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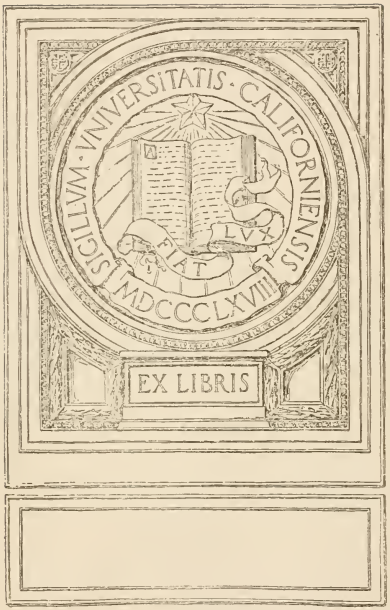
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CARRIERS
IN
INFECTIOUS DISEASES

A MANUAL ON THE IMPORTANCE, PATHOLOGY, DIAGNOSIS AND TREATMENT OF HUMAN CARRIERS

BY

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WITH

A SECTION ON

CARRIERS IN VETERINARY MEDICINE

BY

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To
The Spirit of Science
and
The Instinct of Service

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PREFACE

In writing this book, the author has attempted to prepare a manual on that young but rapidly growing specialty in preventive medicine, which, for want of a better term, may be called carrier work. The subject has been treated as a part of general medicine and surgery, and the book is intended to be of practical value to medical students and physicians, especially those with public health responsibilities. The didactic or text book method of presentation has, therefore, been adopted, rather than the monographic. There are already two monographs on this subject in English: "The Carrier Problem in the Infectious Diseases," by Ledingham and Arkwright, and "Human Infection Carriers," by Simon. The writer's aim is not to compete with these valuable works, but to supplement them. No effort is made to develop the subject historically or bibliographically, except to emphasize certain points or to refer to recent summaries. The idea has been to give a systematic exposition of current medical theory and practice as relates to carriers. Some idea of the amount of work, which has been and is being devoted to this subject, can be gathered from the fact that there are in the catalogue of the Surgeon-General's Library, on typhoid carriers alone, over three hundred references to recorded experiences. An effort has been made to collect, from these sources and from practical experience, the lessons that survive the test of time and trial and thus deserve a place in the program for the future.

The writer has had personal experience with carrier problems from several different angles. On the theoretical side, anyone who in these days works intelligently for the health of groups, as well as of individuals, soon realizes that carriers as well as cases must be considered in any rational and radical program for the control of the infectious diseases. In attempting to study carriers, it was found that animal experimentation afforded a good method of approach, as human carriers are not always available when desired and clinical conditions often cannot be analyzed experimentally.

PREFACE

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Some personal experimental work was, therefore, done on the mechanism of carrier production, and on the possible use of animals in solving carrier problems. On the practical side, it has fallen to the author's lot to investigate the origin of several epidemics in which the carrier possibility was a proved or unproved factor. Considerable laboratory work in the bacteriological diagnosis of carriers, the virulence of cultures, etc., has also been done in the course of routine duties. Clinically, before and especially during the war, I had an opportunity to test the results of surgical treatment of typhoid, diphtheria and streptococcus carriers and am convinced of the value of these measures. During the war, survey and carrier work, which was done on a larger scale than ever before, yielded much new information. Many questions of policy and feasibility were also raised. Some personal experience with such problems has been valuable in orienting the subject. Several years' experience in teaching infectious diseases at the Army Medical School has also emphasized the importance of the subject of carriers in a general course. Altogether, therefore, from personal experience, the author believes that there is a place for a practical manual on carriers. The shortcomings of this attempt are realized, but it is hoped that these pages may assist in a more systematic understanding of the problem and may lead to more effective use of our knowledge.

It is a pleasure as well as an obligation to acknowledge much indebtedness to the staff and organization of the Laboratories of the Army Medical School, under the Directorship of Lieutenant-Colonel Charles F. Craig, and to the Curator of the Army Medical Museum, Major G. R. Callender, of the Medical Corps of the Army.

Carriers exist in the infectious diseases of animals and plants as well as of man, and the comparative or biological method is as valuable in the study of carriers as it is in other branches of medicine. In addition, there are, of course, practical carrier problems for veterinarians and horticulturists. Plants differ in so many respects from man and animals and so little is known about their mechanism of immunity, that this field can not be discussed here with much advantage. Carriers among animals, however, are better understood and are analagous to human

carriers. In fact, all our animal experimentation is a part of veterinary medicine. Moreover, in several of the infectious diseases, animal carriers directly concern physicians. In order to cover this interrelated field, Captain R. A. Kelser, of the Veterinary Laboratory of the Army Medical School, has contributed a section on carriers in veterinary medicine.

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INTRODUCTION

It is common knowledge that the recognition of the infectious nature of many diseases made a new era, both in the theory and in the practise of medicine. On the philosophical side, the parasitology of Pasteur and Koch soon became linked up with Darwin's grand conceptions and has taken its place in the scheme of the struggle for existence and natural selection. On the practical side, the "germ theory" has revolutionized medicine by giving us much new insight into and control over many diseases.

Within the realm of the infectious diseases, the concept of the so-called healthy carrier was also epoch making. It pointed to a new possibility in the outcome of the fight of man against his parasites. The patient may recover with complete destruction of the parasite. The parasite may win with death or disability of the patient. But there may also be a draw with the production of a carrier. The appreciation of this possibility lead to fresh progress in the explanation and prevention of infections. The original observations are accredited to Koch in his work on cholera in 1892–1893. Work on typhoid fever developed the subject and by degrees carriers have been given a regular place in the picture of infectious diseases. Most of our exact knowledge has come from work on typhoid and diphtheria carriers.

It may be accepted that the continued existence of many infectious diseases depends, to a considerable degree, on the spread of pathogenic parasites from apparently healthy and usually immune individuals to susceptibles. The strength of the carrier program rests on the possibility of detecting such parasites and such susceptibles and of keeping them separated. This possibility, however, depends on scientific knowledge and on administrative control, neither of which is complete. In many diseases we have no ready means of determining the virulence of the parasite in the possible carrier or the susceptibility of the possible host. In addition, when we have this knowledge, it is often impossible to apply it practically on a large scale on account of the limitation of

laboratory facilities and because the affairs of life are not run purely for preventive medicine. The carrier program, therefore, admittedly has its weak points. However, with the increase of the exactness of our knowledge and with the generalization of scientific education, social consciousness is calling for more and more carrier work. The specialist and the man on the street are gradually joining their forces for a strong combined attack on the carrier problem.

The greatest need in carrier work at present is the intelligent coöperation of medical men in making a workable synthesis. Too often the bacteriologist knows only his germs, the physician knows only his patient, and the sanitarian knows only the gross situation in the field. Each tries to construct the whole story from his own point of view and as a result the literature contains many assertions, half truths and guesses which hinder real progress. The only way to improve is for all concerned to get closer to the realities and to coöperate with mutual self-restraint.

In view of the increasing importance of the subject, a special terminology is desirable. The term "bacteriophoria" has been proposed to indicate the condition of carrying bacteria. But this term does not include the carrying of protozoa and metozoa and does not cover the science and art of the subject. A more precise word would be *parasitophorology*, or for short, *phorology*. A carrier would be a phore, or a phorist, and a worker on carriers would be a phorologist. While these words might lend themselves to ridiculous developments, such as treponemaphorologist, it appears that phorology and phorologist (medically speaking) might be useful at times and they are suggested for consideration.

A carrier is an individual who harbors and transmits pathogenic parasites without showing the usual evidences of infection. Some carriers show no clinical or pathological evidences at all and are really healthy, but the most important carriers are only apparently healthy, because, on careful examination, they do show signs or symptoms of local infection. Although in some instances the parasites are carried purely mechanically, in the worst carriers they have a home which is usually a slight chronic inflammatory lesion of a mucous membrane. The absence of disease in carriers is due to the fact that the carrier either (1) is in the stage of incu-

bation; (2) has a general but not a local immunity; or (3) is too slightly infected to show symptoms.

Carriers may be classified as follows:

1. *True carriers*
   - A. *Incubationary carriers*—temporary
   - B. *Convalescent carriers*—temporary, chronic and relapsing
   - C. *Contact carriers*—temporary and chronic, primary and secondary.
2. *Pseudo-carriers*
3. *Possible carriers*

1. True carriers. The parasites are pathogenic and virulent. Questions of relative virulence are of course involved and many of them are unsettled at present. The weight of evidence, however, is against sudden changes of virulence and in true carriers, according to actual tests or reasonable assumption, the organisms are of sufficient virulence to infect.

A. Incubationary or *precocious carriers* are infected and infective individuals in the incubation period of various diseases. These carriers are recognized as especially dangerous in the acute exanthemata. They have also been recognized in cerebrospinal meningitis, typhoid, cholera, and other diseases. In some carriers the germ apparently has a "resting" period much longer than the clinical incubation period. Even with the ordinary period of days and weeks, an apparently healthy person may in this way spread trouble in many directions.

B. Convalescent carriers are of three kinds, the temporary, chronic and relapsing.

1. Every case must pass through the temporary convalescent carrier stage and fortunately most cases terminate in this way. There is a clean-up fight between the body cells and the parasite with complete victory for the tissues. Along with convalescence or soon afterwards, the patient is disinfected by immune bodies and phagocytes and does not infect his environment or immediate contacts.

2. A small percentage of convalescents, however, become chronic carriers. These form the bulk of the carrier menace and problem. The microörganisms perpetuate themselves from car-

rier to case and from case to carrier. This is the vicious circle which must be broken to win the fight against infectious diseases.

3. Relapsing carriers. A group of this kind is useful as it covers convalescent carriers who later relapse into cases. Examples of such carriers are found especially in protozoal infections in which the immunity is not as sharp as in bacterial infections. The point of difference between a chronic or latent case and a relapsing carrier is the slowly progressive nature of the infection in cases and a complete balance, even if temporary in carriers. If the carrier conception is broadened to include the infection of one organ within the individual by a carrier lesion in another organ, cases of focal infection can be considered relapsing carriers.

C. Contact carriers or "healthy" carriers are those who acquire the parasite from association with cases or carriers without developing the disease themselves. Such carriers are already immune. Differential diagnosis between a contact and incubationary carrier can be made in most cases only by the outcome. Contact carriers are usually temporary, but may become chronic if there already exists some predisposing chronic focus. Thus, an immune contact carrier with a negative Schick test and an obstructed nasal passage may carry diphtheria bacilli until the deformity is corrected. Contact carriers may be primary, that is, infected by a case, or secondary, infected by another carrier. The importance of pure contact carriers has been exaggerated. Many so-called contact carriers are really convalescent carriers after mild infections, as has recently been emphasized by Craig.

Contact carriers might include also "mechanical" carriers such as surgeons with contaminated hands, but such carriers as well as inanimate objects which carry infection by indirect contact are best considered under personal hygiene and general sanitation. There is nothing distinctive about their carrier relationships.

2. Pseudo-carriers. A group should be made for carriers of non-pathogenic and non-virulent organisms. These may be called pseudo-carriers. In any extensive carrier work suspicious organisms are found which, however, on further examination, turn out to be of no importance. In the meantime, the patient may have been handled as a true carrier. The diagnosis should be changed to that of pseudo-carrier. Such carriers are especially well recognized in diphtheria.

3. Possible carriers. A group of possible carriers may well be made to account for the considerable number of persons who carry organisms of uncertain significance. These organisms at present can neither be proved nor disproved to be of importance, on account of the inadequate state of our knowledge. Under this heading would come many carriers of streptococci, influenza bacilli, and various intestinal organisms. With increasing knowledge this group will naturally disappear as the members of it are distributed among the true and psuedo-carriers.

Convalescent carriers have been called *active* and contact carriers, *passive*. These terms are valuable in emphasizing the difference between the active focus of multiplication in convalescent carriers and the usual absence of a home in the contact carrier, but they are somewhat misleading as all true carriers are active from the point of view of the parasite.

Cases have also been called acute carriers, but this is believed to be an unfortunate use of terms, as it is desirable, on many grounds, to distinguish as clearly as possible between cases and carriers.

Insects which transfer pathogenic microörganisms are often called carriers. In malaria, the mosquito is as an essential part of the carrier mechanism as the formation of gametes in the blood. The final result is also the same, whether typhoid, dysentery or cholera germs are spread by the fingers of a carrier or by the feet of a fly. But the subject of insect carriers, while closely related to that of human carriers, practically, deserves separate consideration theoretically.

From the biological point of view, as has already been pointed out, the chronic carrier state must be considered as the result of a drawn battle between mankind and its parasites. It is personal victory as the invader is restricted to an insignificant position; it is a social defeat, however, as the invader still maintains a foothold and is able to attack new individuals. In other words, chronic carriers are examples of the balance which nature tends to establish in the struggle for existence. The same carrier balance is seen in the whole scale of life from the lowest to the highest forms. Whether in plants, animals or man, parasites are competing with hosts in the infectious diseases and the carrier state is one end result. Neither side wins a complete victory.

The situation is compromised and infection and immunity are balanced against each other. While we accredit nature with marvellous adaptations for the welfare of mankind, it should not be forgotten that a typhoid gall bladder or a diphtheria tonsil represent a diabolical mechanism for the perpetuation of some of man's real enemies. It is the aim of preventive medicine to break up this balance in favour of man.

Work on carriers is another evidence of, and argument for, the socialization of medicine. The extreme individualism of the past is very satisfactory to the favored few, but it does not take into consideration the welfare of the many who make up the strength of the nation and who have a way of getting what they want and need. The care of the individual case is a unit of medical attention, but it is only part of an adequate program for the control of infectious diseases. The carrier is also a problem which requires special handling, technical and administrative. In addition to diagnosing and treating the case, physicians should learn to diagnose and treat the carrier and keep pace with the increasing social demands for the application of practical measures. As physicians and citizens we need to realize, once for all, that while in some respects the individual is an ultimate unit, in others, he is only a part of higher units, the family, the community, and the nation, and he cannot exist without them. Hence, medically as well as biologically, the interests of the whole, that is, of the race, are greater than those of the individual parts. On the other hand, it is the individual who, in the long run, profits from the welfare of the group.

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PART I
GENERAL CONSIDERATIONS

CHAPTER I

Importance

The importance of carriers is two fold. In the first place, chronic carriers constitute more or less permanent reservoirs of pathogenic microörganisms. Cases are usually acute and the danger of spread of infection is limited to days. The chronic carrier, however, is able to infect his environment or contacts for months or years. While the acute case excretes more germs and probably causes most cases after an epidemic starts, the carrier is able to start the epidemic itself by storing the germs until seasonal or other conditions are favorable for an outbreak. Some workers claim that in this way a carrier will always be found as a connecting link in any considerable series of cases. According to Vaughan, one of the principal contributions of bacteriology to epidemiology is the teaching about carriers.

Soon after the recognition of the infectious nature of many diseases, it was thought that the environment of cases was heavily contaminated with germs. In this period efforts were directed especially at the disinfection of water, milk, clothing, and fomites. It was soon learned, however, that many pathogenic germs live outside the hosts only a short time and that, while much can be done by sanitation, the contact avenue of infection remains largely open. Attention was then focused on the case itself. It was taught that if all acute cases were detected early and isolated the streams of disease would dry up. But again it was soon found that, while much can be done along these lines, there is still a good sized flow from the carrier reservoir. At present, therefore, much attention is being devoted to this other personal source of infection.

The second reason why carriers are important in preventive medicine is, of course, the fact that they are apparently and practically healthy. The case, confined to bed or to a sick room, limits the spread of parasites, consciously or unconsciously. The carrier, however, usually unaware of his condition, moves about freely, infecting his environment or contacts without notice. It

is this circumstance which has made the subject so dramatic to the laity and so serious to the profession.

The importance of carriers varies in different diseases. In a few instances, such as typhoid, enough information is becoming available to actually estimate the number of cases due to carriers as compared with those due to other cases. In other diseases the exact relative importance of carriers is not so well known, but the carrier has a definite place in the epidemiology of cholera, dysentery, diphtheria, cerebrospinal meningitis and malaria. The organisms can be identified and traced. In some diseases, such as smallpox and measles, carriers are not important, according to usual statements. This position is based on epidemiological evidence which may or may not have been rightly interpreted. Until more is known about the organisms causing many diseases, no adequate statements can be made about their carrier aspects.

There is undoubtedly a tendency at times to overestimate the importance of carriers. Other cases, including mild ones, should be considered as a cause of a given case before a carrier is suspected. It should also be remembered that many so-called carriers are really pseudo-carriers who are simply parasitized by non-virulent organisms. Those organisms may resemble pathogenes morphologically and a presumptive diagnosis may be made. But virulence tests nearly always show that some suspected organisms have no significance. Hence, while recognizing the real importance of the true carrier as a reservoir of pathogenic parasites and as an unadvertized danger, the practitioner of preventive medicine must recognize the relative importance of carriers in different diseases and the existence of the pseudo-carrier.

On the other hand, there is in some quarters a tendency to belittle the carrier program as ineffective. This tendency, I believe, is a mistaken one. It is based simply on our insufficient knowledge or inadequate control. We should not give up the advantage won by the known existence of carriers of pathogenic organisms because we cannot always assign them a definite place in the unknown whirl of atoms or control their activities. It should be realized that only rarely has the carrier plan of attack on an infectious disease been given a thorough trial. A certain amount of work has been done, but it is usually not complete and

radical because of the limitation of facilities and control. The plan breaks down because the work is too extensive. This circumstance has lead some workers to minimize the program. It is impossible, however, to sucessfully attack the principles of phorology. The only question is how far the details should be carried out. As laboratory facilities become more numerous and reliable, and as scientific control of events becomes more established, the proper amount of attention will be given to this rational plan of attack on our competitors in life.

The importance of carriers can be realized by considering, first, the percentage of cases which become convalescent carriers, then the percentage of contacts who become contact carriers and then the percentage of both kinds of carriers in the general population. Best of all, however, is the actual demonstration of the spread of organisms by a carrier in a specific group of cases.

The study of carriers is valuable to the medical student as it shows him something of the biological background of disease which has been so useful in orienting the medical sciences. Carriers form a link in the natural history of disease. To understand them is to acquire a liberal medical education and to control them is to aid in defending and extending civilization. The different phases of carrier work involve anatomy, physiology, bacteriology, parasitology, pathology, immunology, medicine, surgery, sanitation, hospitalization, quarantine and follow up service.

The general practitioner needs to know the best teaching about carriers as he is in the most strategic position to break up the parasitic balance in favor of man. Too often, either through ignorance or limited view of responsibility, this opportunity is lost. Patients are carried through a severe infection with skill, but are turned loose, without release cultures, to inflict the same disease on others. By insisting on release examinations in any case whose cause can be found by such examinations, the practitioner can have the satisfaction of practising preventive medicine at the most critical period. If the examination is negative, the case can be completely closed and the patient is better satisfied. If the examination is positive, the patient may be a temporary convalescent carrier and may clear up with a short extension of convalescence. If the case becomes a chronic carrier, he can in

some instances be cured and at least he can be instructed in personal hygiene. If he does not respond to social obligations, restrictive measures must be applied. In diphtheria, this ground is already covered by regulations, but in several other diseases the practitioner decides what shall or shall not be done. It is much easier to ignore this subject, but microörganisms can not be trusted. There will be no general advance in the prevention of many diseases until the general practitioner helps by detecting and handling convalescent carriers.

Most of all the public health official must realize the importance of carriers as his position is due to a social demand for supervision of the health of groups, among whom carriers are sure to be found. He must officially be in position to diagnose and handle carriers. Carrier work among private physicians is largely voluntary and depends on the degree of social consciousness of the individual. The public health official, however, is paid to be socially minded.

The organization includes, first, the laboratory for the discovery of carriers, and second, regulations to secure appropriate action. The needs of the laboratory are more fully discussed under the heading of diagnosis. It is sufficient to say here that nowhere can the laboratory facilities be considered adequate for the work that might be done. Of course the question is an economic and social one. Do the results justify the expense and trouble? The answer here as elsewhere seems to be that, as scientific knowledge increases, there is an increasing demand for its application in the amelioration of human life.

On the administrative side, there are many perplexing questions of policy in handling carriers. The uncertainty of our knowledge in some diseases and the fallability of laboratory workers often add to the confusion. But one point should be kept clear. The interests of the group of race are supreme over those of the individual. This decision has been handed down by Nature and by Society and other decisions must conform. The interference with the individual should be as slight as possible, but there should be no question about the principle that governs.

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CHAPTER II

Pathology

The pathology of carriers includes specific lesions and a general or local immunity. The anatomical basis is an important factor, but immune reactions underlie the phenomenon as a whole. While there are many unknown elements in the equilibrium between host and parasite as seen in carriers, there is also available much actual knowledge or suggestive information.

In the *temporary contact* carrier there is probably no demonstrable lesion. The organisms apparently live and multiply for a short time on mucous surfaces and then die off or are washed away by the secretions. The tissues are immune and in the absence of actual proof the most that can be imagined is a slight preëxisting lesion which produces an increased secretion of mucus as a temporary focus.

In the *chronic* contact carrier, however, some definite preëxisting lesion is often found upon which the parasite becomes ingrafted. There is probably a slight re-infection in the immune host. As soon as the cause of the primary lesion is removed, as, for example, by extraction of a foreign body or the correction of a deformity, the carrier state becomes temporary again. The carrier lesion, in itself, is here again very superficial.

The lesion of the *incubationary* carrier is of course the slight inflammation produced in the tissues by the first invasion of the parasite and its early multiplication. Natural lesions of this kind are rarely obtained for study, but experimental lesions fill in this gap. In the early stages of infection, the microörganisms are found on the epithelial surfaces, penetrating between the cells (Cecil and Blake). There is some capillary dilatation and oedema and a migration of leucocytes. Once past the epithelial barrier the organisms spread along the lymphatics, multiply and break out again through the epithelial covering into open spaces. The course of the lesion is then the usual one for the specific organism. From the carrier point of view, the important fact is that, during

this early period, there is often the greatest multiplication of the parasite and hence the greatest danger of transmission.

The lesion of the *chronic convalescent* and relapsing carrier is the most definite one. It is also the most persistent, the most dangerous and requires the most treatment. The lesion is a small surviving infection in a generally immune host. It dates back to the original attack and has survived the processes which have protected the individual as a whole. The organisms are walled off or protected from the immune mechanisms and live on indefinitely —as balance is reached. The lesion may be slight, even microscopic, but has been found with great regularity in the best known carrier conditions.

There are two especially important sites of chronic convalescent inflammation—the tonsil and the gall bladder. Other similar foci occur in other parts of the body, but the lesions of these two organs may be taken as types, one of the large field of respiratory carriers and the other of the large field of intestinal carriers. Chronic tonsillitis and cholecystitis should, therefore, be considered in some detail.

Chronic tonsillitis. This lesion explains the existence of many carriers of virulent diphtheria bacilli and hemolytic streptococci. It is probably also primarily or secondarily responsible for carriers of pneumococci, meningococci, staphylococci, influenza bacilli and the organisms of Vincent's angina. Filterable viruses are also carried in the tonsils.

One of the recognized functions of the tonsils, adenoids and other lymphatic structures of the upper respiratory and alimentary tract is to help protect the body from infection. Pathogenic bacteria are picked up by these phagocytic lymphoid structures and an attempt is made to destroy them, as in acute tonsillitis. This function is undoubtedly a valuable one and according to the general consensus of opinion should be preserved early in life. In many cases, however, this function becomes perverted. The tonsil is unequal to its task and the microörganisms, instead of being killed, find a permanent home. The policeman, instead of arresting the criminal, is forced to become an accomplice. Under these circumstances the tonsil becomes an individual and social liability rather than an asset. It is

often best to lose the perverted protective function by removal of the organ or by X-ray treatment.

The average tonsil is not normal in the sense of healthy lymphoid tissue covered with intact epithelium. Almost every

FIG. 1. SECTION OF TONSIL OF CHRONIC DIPHTHERIA CARRIER. × 50
Shows loss of epithelium and fibrinous exudate in tissue

tonsil which is examined shows some disintegration of epithelial covering with exudation and signs of inflammation, due to infection with various pathogenic parasites (fig. 1). In addition to these and as illustrating the favorable conditions for parasitism,

various other harmless parasites are found, such as amoebae and leptothrices. An undescribed yeast-like organisms with no inflammatory reaction about it is present frequently in sections (fig. 2).

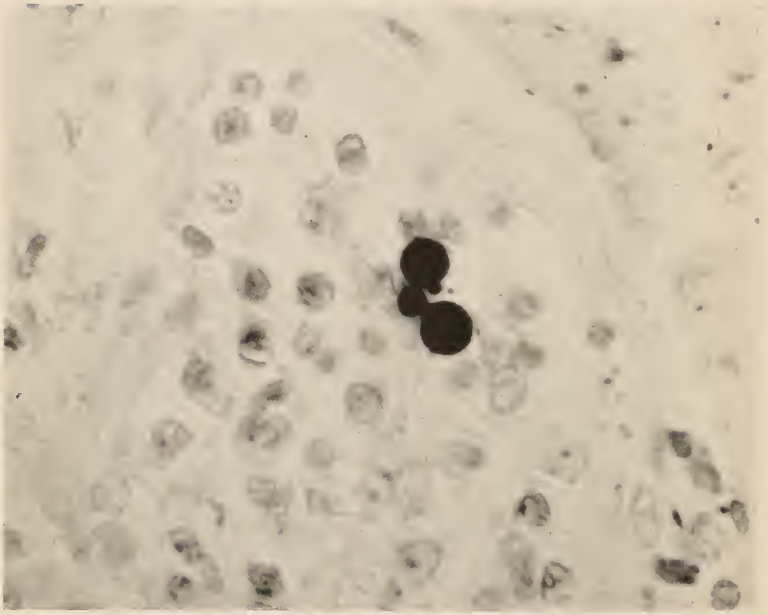

FIG. 2. UNIDENTIFIED YEAST-LIKE ORGANISMS FREQUENTLY FOUND IN SECTIONS OF TONSILS. × 400

MacCallum stain. Note absence of reaction around parasites

The tonsil, therefore, is often a hot bed for microörganisms. The crypts become incubators instead of disinfectors. Heat, moisture and food are supplied by the body while the antiseptic action of the tissues and body fluids is neutralized by poor drainage. The structure of the crypts with their blind ends, tortuous

channels and "underground" connections make an ideal nest or home for these parasites (fig. 3). With such an organ as this at the gateway to the body, it is easily realized that the chances for carrier production are particularly good. Temporary and chronic convalescent carriers are especially apt to develop.

The same situation exists with less frequency in lesions of the sinuses, turbinates, septum, gums and other structures of the nose and mouth.

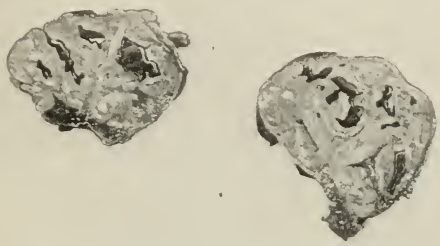

FIG. 3. PHOTOGRAPH OF TONSIL INJECTED WITH LAMPBLACK AND PARAFFIN TO SHOW CRYPTS

"Underground" connections are emphasized. Preparation by Sturm

Chronic cholecystitis. The gall bladder has of course an entirely different function from the tonsil, but, in its carrier relationship, the entire gall bladder may be compared to a crypt of the tonsil. The wall is slightly invaded in a chronic process and the contents consist of a rich culture of typhoid or cholera bacilli. Apparently the bile neutralizes the antiseptic effect of the leucocytes, mucus and serum, while the addition of these substances increases the nutri-

tious value of the bile. The result is a very effective multiplying and distributing agency.

Much work and speculation have been devoted to the subject of the mechanism of gall bladder infection. The possibilities of infection are (1) ascending, through the common and cystic ducts from the intestine, (2) embolic, in the blood and lymph vessels of the bladder wall, (3) descending, through the bile from the liver. Any of these methods may occasionally occur, but ascending infection is apparently rare. Evidence from some experimental work in rabbits seems to favor an early small embolic lesion of the wall with subsequent general infection of the contents and wall (Meyer). Other experimental work favors the descending route, as large numbers of bacteria are excreted from the blood by this method and an inspissation of bile is known to occur in the bladder. This theory also draws some support from the fact that a large number of carriers occur among women in whom biliary stasis is more frequent. The important fact is that, whatever the earliest lesion, the end result is a general mild catarrhal inflammation of the wall with infection of the contents of the cavity.

The cholecystitis starts as an acute mild process during the original disease and persists indefinitely. When examined after operation or autopsy, these gall bladders have a thickened wall and altered contents. The ordinary uniform brown bile is replaced by a yellowish or whitish fluid with sediment of purulent flakes. One or more gall stones are present.

The wall shows a general catarrhal inflammation. Ulceration does not occur except possibly early and no lesions of the wall are found except in the submucosa. Here there is a uniform collection of lymphocytes indicating a reaction to infected contents (fig. 4). The epithelial wall may show nests of bacilli (fig. 5).

The carrier state can be produced experimentally in a certain percentage of rabbits by intravenous injection. The gall bladder lesions are of value in attempts at chemotherapy and for demonstration. Gay and Claypole state that by a special technique they are able to make 100 per cent of carriers. Ordinarily, about 30 per cent of carriers result from the injection of sub lethal doses. Freshly isolated cultures are most effective.

In some carriers the surviving lesion seems to be confined to the gall bladder as excision of this organ results in bacteriological cure. In others, however, there must be other lesions in other parts of the biliary system, probably higher up in the smaller bile capil-

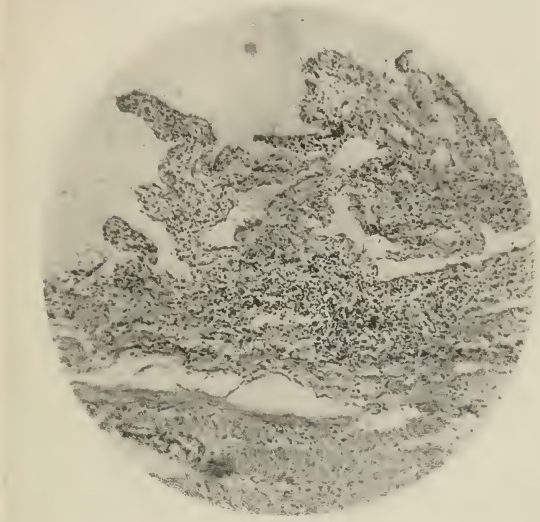

Fig. 4. Section of Gall Bladder in Human Typhoid Carrier. × 70

The section shows that the lesion is confined to the mucous membrane of the bladder. There is a mild general catarrhal inflammation with migration of leukocytes into the submucosa.

laries, because cholecystectomy, in some carriers, does not result in cure. No practical way of determining the existence of exact location of this lesion is available at present. These lesions of the liver in carriers are not well understood but they may originate in the so-called focal necroses which are really emboli of endothe-

lial cells. In experimental work, infection of the smaller bile capillaries occurs with the production of multiple cysts resembling a bunch of grapes.

FIG. 5. DRAWING OF SECTION OF GALL BLADDER IN EXPERIMENTAL TYPHOID CARRIER STATE IN RABBIT. × 800

Nest of typhoid bacilli is seen in epithelial coat and the collection of leukocytes is seen in the submucous coat.

The other lesions of intestinal carriers are chronic ulcers of the intestines which will be discussed under dysentery.

The lesions of the urinary carrier are much the same as those of the intestinal carrier. The lesion is really in the hilum of the kidney—a chronic pyelitis with secondary cystitis. The lesion is a surviving one and the same questions of pathogenesis arise as in case of the cholecystitis.

In addition to the actual lesion, the general state of immunity of the body is of great importance in carriers. In incubationary carriers there is naturally no immunity or only a beginning one. In convalescent carriers there is a general immunity, but not a local one. In some instances the carrier state probably keeps up an immunity by continuous vaccination. The organisms in the focus stimulate the formation of immune bodies such as agglutinins, opsonins, bacteriolysins and complement fixing bodies. These are not present regularly or in strong concentration and suggest a balanced immunity. In relapsing carriers the balance is delicate and easily upset, especially in protozoal infections. In true contact carriers there is a general or local immunity. No evidence is found of active immune processes.

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CHAPTER III

Diagnosis

The adequate diagnosis of a carrier involves (1) the identification of the specific parasite, or of specific immune substances; (2) the location and significance of the focus in the host; (3) the relation of the carrier to his environment and contacts. The diagnosis is, therefore, a combined one depending on laboratory, clinical and epidemiological work and should be accomplished by "coöperation" rather than by "competition" between the pathologist, the physician and the sanitarian. Of course, some one gifted and energetic individual may in turn find the germ, examine the patient and follow the trail in the group. This has been the most common method in the development of the carrier work and undoubtedly it is best for some one person to gather up all the threads of the story. As the whole carrier movement started in the laboratory, the laboratory specialist often takes the lead, or is expected to do so. But the work has now reached the stage where more organization is needed. No one person can do justice to all aspects of the situation. The requisite for effective work is the intelligent coöperation of all concerned.

In the laboratory diagnosis, the finding of the specific organism is usually the aim. Details of suitable methods are given later under each infection. In general it may be said that specific diagnosis is more difficult in carriers than in cases. There are usually more individuals to be examined. The organisms are usually less numerous and may be more mixed with other organisms. In addition, there is more doubt about virulence and, if virulence tests are available, these must be made. There are also increasing complexities of groups and subgroups which must be considered.

In some diseases a tentative diagnosis can be made on the presence of antibodies, which are as specific as the parasite itself. Of the antibodies, the agglutinins are the easiest to detect and have been most used. As far as is known, they are as reliable as

any others in carrier work. Agglutination is an especially valuable measure in dealing with veterinary carriers. Allergic skin tests have been proposed as an aid in detecting carriers. If reliable, such tests would be of great value. As yet, however, they are not on a practical basis in human medicine. Naturally all these immune reactions are indications only of infection. They do not distinguish between a case and a carrier, but they may aid in the final diagnosis.

In addition to attempting to find the parasite or evidences of its presence, the laboratory may be called on to determine the susceptibility of possible hosts or at least to supply the biological materials, if such tests are practicable.

It is evident that, with this primary dependence on laboratory methods, the work of the laboratory must be reliable. The clinical check is slight at best. Hence, the personnel and equipment of a phorological laboratory must be even better than those of a laboratory of clinical pathology. The pure technician is, therefore, of limited value in carrier work. The type needed is the specialist who has emerged from a general medical background. As has already been said, laboratory facilities have practically never been sufficient for the work which might be done. If carrier work is worth while, as it seems to be, more support, financial and moral, should be given to the laboratory.

The clinician can aid in the finding of the parasite by picking out suspects for examination. Meningococcus carriers are more apt to be found among persons with large amounts of mucus in the nasopharynx and streptococcus carriers among those with large tonsils. Typhoid carriers sometimes have local signs or symptoms of cholecystitis. The personal history of disease is also often suggestive. Another useful field of clinical activity exists in the actual securing of a satisfactory specimen for laboratory examination. Much lost motion and confusion results from the examination of poor specimens. To obtain a good specimen from the tonsils, nasopharynx, sinuses, duodenum, or ureters requires considerable technique which should be furnished by the clinician or by his organization of technical assistants and nurses.

After the presence of a virulent organism in the body has been established, a clinical survey is necessary to locate the focus, to

decide the diagnosis between a carrier and a mild case or to classify the carrier. This work can be properly done only by a clinician. Altogether, therefore, the physician has an important part to play in the diagnosis.

Like the clinician, the epidemiologist can assist in the diagnosis by picking out the most suspicious individual or group for examination. Of course the possible contacts and sources of infection are often innumerable and the most effective method would be a complete examination of all persons. There would then be available a complete record of their parasitological status. But such a state of affairs is for Utopia, not for our work-a-day world. The medical Sherlock Holmes can often get a clue from the general situation which can be followed up in the laboratory. The number to be examined can often be narrowed so that a few persons can receive especial attention. This result requires, of course, the usual epidemiological investigations of personal habits, occupation, journeys, and so forth.

When the carrier is once diagnosed, individually, the epidemiologist must be depended on to make the social diagnosis. The finding may mean much or little according to circumstances. Hence, in the last analysis, the epidemiologist should be the coördinator in carrier work.

CHAPTER IV

Treatment

The treatment of carriers has one unusual factor. Unlike the case, the carrier must be convinced that he needs medical attention. The correction of the trouble also has more social than individual value. Hence, self-interest is often directly against any treatment. The situation should be handled along the following lines. Carriers usually have chronic infections. These may become acute at times and make more trouble. Moreover, all current medical teaching favors the removal of chronic foci of infection for the good of the individual. Hence, a carrier has personal reasons for being treated. In addition, the interests of society are paramount to those of the individual. The individual should recognize his social obligations and as far as possible not do harm to others. If he is unwilling to accept this point of view he may be forced to it. As was shown in the great war, society will not tolerate individual action which is anti-social in emergencies, and cases of infectious disease are more and more being regarded as emergencies. Reason is effective with many carriers discipline with others, but some can be handled only by force.

The treatment of carriers includes technical methods, instruction in personal hygiene and administrative or legal measures.

The technical treatment of infections as applied to carriers consists of the following procedures:

a. Good hygiene, local and general, to assist in the natural processes of combatting microörganisms. These measures are especially valuable in handling temporary contact carriers, such as meningococcus carriers.

b. Specific anti-microbic treatment, which consists of the use of vaccines and sera. These measures in general have been disappointing, but analogy and partial success keep alive the possibility that these measures may some time be effective. As the focus in convalescent carriers has persisted in spite of a general immunity which has practically cured the patient, little effect

might be anticipated from specific vaccines or sera. In fact, experience has shown that typhoid vaccination does not cure typhoid carriers with any regularity and diphtheria antitoxin and vaccine do not cure diphtheria carriers. The whole subject of the therapeutic use of vaccines is in such a state of uncertainity that definite statements cannot be made.

The use of non-specific vaccines has also been tried with the idea of producing a reaction which might clean up a carrier lesion in the same way that it sometimes affects other chronic foci. This measure may have turned the balance in some carriers, but many are resistant.

c. The local use of disinfectants. This is a logical procedure but is not completely successful in practise. The number of organisms may be reduced and, with this reduction, the danger of transmission may be lessened, but cure is not regularly attained. During the war, elaborate devises, such as gassing chambers, were used for the large number of carriers. The consensus of opinion is that specific action was not proved. In some instances, the antiseptics seemed to injure the natural resistance of the mucous membrane and the organisms grew out in pure culture.

d. Specific chemotherapy. The carrier has been a particularly attractive subject for workers in chemotherapy and a great many compounds have been tried experimentally, especially in gall bladder infections. At present it cannot be said that any one compound has won its way clinically except the arsphenamine series in spirochete carriers. Mercury, quinine, emetine and antimony of course have their place in the treatment of carrier infection.

e. The most successful local method of treating carriers is the removal of the focus by surgical operation. This measure has been successful in over 50 per cent of typhoid carriers and in over 80 per cent of diphtheria carriers. Under this head come also corrective measures, such as the removal of foreign bodies and the opening of obstructed air passages. X-ray and radium have been tried as a substitute for surgery. They have failed to influence gall bladder lesions, but in some instances contract the tonsil and may be a method of choice under certain circumstances. Unfortunately the lesion may be reduced but the organisms may

persist. Repeated treatments may be necessary and, for prompt and permanent results, tonsillectomy is preferable.

The results of surgical treatment of carriers confirm the conclusion drawn from experimental and pathological study of the subject, namely, that the chronic carrier state is really an infection which is usually sharply localized.

The surgical treatment of carriers calls for coöperation on part of the surgeon. The diagnosis is usually made by physicians and the surgeon is asked to give technical assistance only. At the same time, he should accept the program. Some surgeons decline to operate except on cases, but this is a limited view of the possibilities and responsibilities of surgery.

Aside from purely technical treatment there is with carriers an especial reason for "treating the patient as well as the disease." The carrier is subject to isolation and ostracism. During the war, in one battalion, the men threatened to kill a meningococcus carrier who had, of course unconsciously, infected and caused the death of several companions. Some individuals cannot understand the situation and become depressed and psychoneurotic under quarantine and continued examination. The circumstances should be clearly and simply explained and an effort should be made to stimulate the individual's social morale. His inconvenience is for the good of the greatest number. In suitable cases a radical cure should be attempted. Otherwise a carrier should be instructed in personal hygiene and be examined at intervals and inspected for observance of rules. In dealing with irresponsible persons, forcible detention may be necessary as a last resort.

In the handling of carriers, personal hygiene must be given a prominent place, as intelligent coöperation will accomplish results when treatment fails or when quarantine is impossible. The object of personal hygiene in this case is the social one of protecting others, but when properly approached, few individuals will fail to respond to some social obligation.

If carriers are quarantined in hospitals, the number may be so large that a special ward for isolation and observation may be necessary. In this case the social service and vocational workers should assist in keeping up morale. The "working" quarantine principle should also be applied.

Prevention. The prevention of the development of carriers is a part of preventive medicine, as well as their detection and cure. Specific measures for this end are limited at present, as too little is known about the mechanism of the production of carriers and too few means of influencing that mechanism are at hand. Already, however, we know that deformities of the nasal passages and the tonsils predispose to carrier conditions. Hence, there is an additional argument for good hygiene of the nose and throat. It is possible that in typhoid fever, the antiseptic action of the bile may be increased by diet or by antiseptics. It is also possible that the more severe the disease, the more likelihood there is that a carrier state will result. In this case there would be an extra argument for good nursing.

Of course, carriers can be prevented indirectly by preventing cases. Carriers can also be prevented in a sense by curing them. But the actual prevention of carriers by a complete cure of the infection should be a recognized object of the treatment of a case. The discharge of a patient without release cultures and appropriate action is as unprofessional as the treatment of a case without a knowledge of the diagnosis.

Altogether the handling and treatment of carriers calls for the "do the best you can" philosophy. The subject is so full of difficulties that the clean cut, radical and dramatic program, of which we are all so fond, cannot often be realized. On the other hand, the actual program is not an apologetic one, but has deep roots in evolutionary history and practical experience.

The present day efforts at improved organization and standardization should include carrier work. The kind, number and intervals of diagnostic and release cultures should be more uniform. Periods of isolation and quarantine should also be revised in the light of increasing knowledge. Most of all, more standard and general rules for the handling and disposition of carriers are needed. At present each state or smaller unit has its own rules or no rules, while what are needed are interstate or national standards. National medical societies, especially those devoted to public health, have a responsibility for initiating such standards.

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PART II
SPECIAL DISEASES

SPECIAL DISEASES

In considering the phorology of each of the most important infectious diseases it is useful to classify these diseases according to their relation to the basic biological necessities of life. These necessities are of course self-preservation and self-perpetuation. Self-preservation, or continued metabolism, calls for the intake of food and drink and the excretion of waste products, for the intake of oxygen and the outgo of CO_2, for the circulation of these and other substances and for the control and correlation of the vital reactions. Self-perpetuation of course depends on sexual intercourse. It also necessitates the recognition of the family as the primary social unit.

In the course of evolution, parasites have become engrafted on these functions and the carrier aspects naturally form only a part of the infection as a whole. The classification roughly covers the avenue both for the intake and outgo of the parasite. Thus we have alimentary, respiratory, circulatory and sexual diseases. Among the diseases of the nervous system or correlating mechanism there are no clear cut carrier problems per se as there is no natural outlet. The "master tissues" are also well protected from direct efforts of the environment such as insect bites. The advantages of this grouping are that similar specimens are necessary for the diagnosis of carriers and that similar means for the prevention of carrier action are used in each group. Comparison or contrast helps to emphasize the important points.

It should be understood, however, that this classification is primarily a practical and not an academic one. The diseases are not strictly limited to any one anatomical or physiological system. Moreover, the natural parasitic order is not observed as one and the same group may contain diseases due to either bacteria, protozoa and to helminths. In short, the object is practical and medical rather than purely scientific.

A. The Alimentary Group, Chapters V, VI, VII and VIII, includes those diseases whose parasites enter the body chiefly in

food and drink and escape in the intestinal contents—the typhoid fevers, cholera, the dysenteries and helminthoses.

B. The Respiratory Group, Chapters IX, X, XI, XII, and XIII, includes the large number of diseases whose specific parasites enter and escape from the body chiefly through the nose and mouth. The most important members of this group are diphtheria, meningitis, pneumonia, influenza, colds, all the acute exanthemata, poliomyelitis, tonsillitis, and other streptococcus infections, Vincent's angina, sinusitis, bronchitis and the other "common respiratory" infections.

C. The Blood Group, Chapter XIV, might also be called the insect transmission group, as the parasites live chiefly within the blood vessels and entrance and egress are possible only by puncture of the vessel wall. It is desirable, however, not to confuse insect carriers with human carriers. The most important diseases from the carrier point of view are malaria and filariasis.

D. The Sexual or Venereal Group, Chapter XV, includes the diseases whose parasites enter and the leave the body chiefly by sexual intercourse.

CHAPTER V

The Typhoid Fevers

The typhoid fevers include the classical type, the more recently differentiated types of paratyphoid A and B, and the latest, C. The carrier relationships are apparently the same in all, with the exception of some forms of infection with Para B bacilli which more nearly resemble bacillary dysentery.

The importance of carriers in this group is well established. Our knowledge of carriers was worked out largely in typhoid and there are on record many dramatic and clean cut instances of the rôle of carriers. The number of cases due to carriers has been estimated by different observers as from 9 to 50 per cent. This percentage is believed to be on the increase, as sanitation and hygiene are reducing infection from cases, but are not so effective against contact infection by carriers.

Carriers are especially apt to contaminate food because 80 per cent of carriers are women. According to Sacquepee, women make up only one-fifth of cases, but three-fourths of intestinal carriers. Carriers among children are said to be rare. Close contact such as occurs among crews on shipboard has been especially favorable for demonstrating the dissemination of bacilli from a carrier. Urinary carriers are about one-tenth as frequent as intestinal carriers and apparently occur more frequently in males. Genuine instances of combined urinary and intestinal carriers are very rare.

Carriers in the general population include of course incubationary, convalescent and contact carriers. The relative and total number of these carriers will depend on the previous amount of typhoid; the age and sex group, etc. In general the number is much less than 1 per cent, and is unquestionably diminishing on account of the reduction of cases. During the war, the examination of about 30,000 food handlers in the Army showed less than 0.1 per cent of carriers among young healthy males.

No satisfactory statistics exist on the relative proportion of different kinds of carriers. "Incubationary" carriers and "contact" carriers have been found in epidemics, but careful clinical surveys, including the examination of the duodenal contents, are usually lacking. The most instructive results have come from a study of convalescent carriers. It has been estimated by Gay that

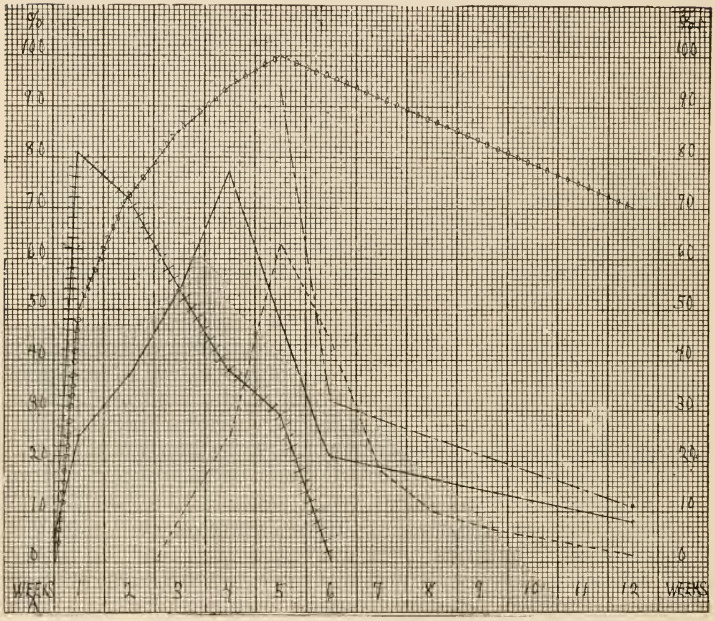

CHART A. DISTRIBUTION OF TYPHOID BACILLI IN CASES AND IN CONVALESCENT CARRIERS

Percentage of bacilli found in blood +++++
Percentage of bacilli found in urine - - - - - - - -
Percentage of bacilli found in feces ————
Percentage of bacilli found in duodenal contents — - — -
Percentage of agglutination reactions o–o–o–o

7500 convalescent intestinal carriers are being yearly added to the population in the United States.

In order to illustrate the percentage of different kinds of convalescent carriers, charts A and B have been prepared which show the distribution of typhoid bacilli in the body in cases and in temporary

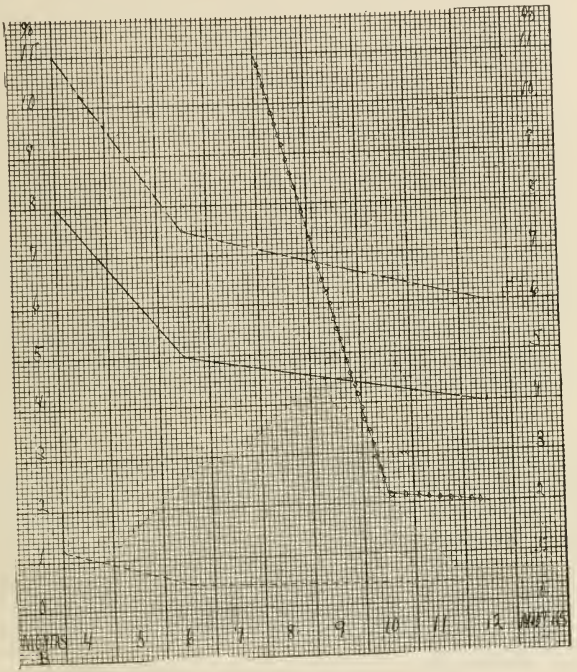

Chart B. Distribution of Typhoid Bacilli in Cases and in Convalescent Carriers

Percentage of bacilli found in blood +++++
Percentage of bacilli found in urine - - - - - - -
Percentage of bacilli found in feces ————
Percentage of bacilli found in duodenal contents — - — -
Percentage of agglutination reactions o–o–o–o

and chronic convalescent carriers. The agglutination curve is also given. The data has been largely taken from Hiss, Zinsser and Russell's Bacteriology, from Gay's monograph and from Garbat's recent work on duodenal cultures. There are several gaps which have been filled in tentatively from the author's experience.

As will be seen, the charts can roughly be divided into four parts. (1) The first month shows the active case, (2) the second month shows clinical convalescence with the occurrence of temporary carriers, (3) the next four months shows the spontaneous cure of many temporary carriers, (4) the next six months shows the persistence of chronic carriers and the fall of the agglutinative curve to a permanent level.

Cultures of duodenal contents during the disease have not been made in any considerable number, but the percentage of cases with bacilli in the duodenum must be very high. During convalescence, according to Garbat, 50 per cent more carriers are detected by this method than by ordinary examination of the feces.

The curves may drop slightly after six months, but most of these chronic carriers persist as far as is known indefinitely. Carriers of at least thirty years duration are recorded.

PATHOLOGY

In incubationary and pure contact carriers there is no definite carrier lesion. The bacilli live and multiply in the intestinal contents for a short time, and then in the incubationary carrier invade the intestinal wall and in pure contact carriers pass out of the system entirely. Various ingenious theories have been devised to explain permanent contact carriers, but a fair consideration of the lesions will lead to the conclusion already expressed that such so-called contact carriers are really convalescent carriers after mild infections. It is an instructive fact that pure contact carriers do not give an agglutination reaction.

In chronic convalescent carriers permanent lesions occur in the ducts of two chief excretory organs, the liver and kidney. Chronic inflammations due to typhoid bacilli exist in other parts of the body, such as the bones, but strictly speaking these are not carrier lesions because there is no natural outlet. It might be thought

that Peyer's patches would be a favourable site for chronic ulceration, but this is not the case. Purely intestinal lesions rarely make a basis for carriers, and pathologically the term "intestinal" carrier should not be used unless such a lesion is demonstrated. The great majority of intestinal carriers are gall bladder or bile duct carriers. Similarly, from the pathological point of view, a pure urinary carrier probably does not occur. There is a definite lesion usually in the pelvis of the kidney with secondary pyelitis and cystitis. Other chronic foci in the genito-urinary apparatus have been considered possible but have not been demonstrated.

As was said in Chapter II, the pathogenesis of these lesions, especially that of the gall bladder, has been occasion of much speculation, many experiments and various conclusions. The exact steps of the process are not yet fully agreed upon, but the end result is well recognized. The explanation is not entirely an academic question, because the success of therapeutic attack may depend on mechanism of the lesion, whether produced through the bile or through the blood. In any case, there is an unfortunate neutralization of the natural defenses of the body. The bile destroys the complement and helps neutralize other antibodies while the serum and mucus neutralize any antiseptic action of the bile.

These carrier lesions date back to the original attack as mild complications which are usually unnoticed. At autopsy on cases dying of toxæmia, some cases of mild cholecystitis are found with definitely inflamed walls. Typhoid bacilli are present in the bile in all cases, but these early cases with lesions are the ones which later develop into carriers.

Carrier strains of the organism do not differ in any known way from strains from cases. There is no simple test for virulence or pathogenicity, but typical human infections have occurred from accidental contamination of the mouth with carrier strains.

DIAGNOSIS

The final diagnosis must necessarily be made by laboratory methods, but the personal history, a clinical examination, or epidemiological evidence may suggest a tentative diagnosis. Many carriers give a good history of the original attack or of some

suspicious illness. Some complain of occasional soreness or tenderness over the gall bladder and give general evidence of being below par. One or more individuals may be put under suspicion by the circumstances of the epidemic.

The laboratory diagnosis is a bacteriological one, but a serological examination may be suggestive. Over 50 per cent of carriers give the agglutination test or Widal reaction as an indication of their chronic forcus. The serum titre is usually about 1:40. This test, however, has little value in early convalescents and in those who have recently been vaccinated against the disease.

The bacteriological diagnosis consists in isolating and identifying the typhoid organism concerned. Usually the feces and urine are examined. A single examination of stool is not conclusive; even in the urine the findings may be irregular. A single examination of duodenal contents is much more conclusive. The bacilli, if present, are in more nearly pure culture than after being mixed in the contents of thirty feet of intestine. Conclusive results can be obtained, according to Garbat, by examining two consecutive specimens of duodenal contents, two consecutive specimens of feces and two consecutive specimens of twenty-four hour urine.

On the occurrence of a case or cases which cannot be explained by other methods of infection, a search for carriers is indicated. The circumstances are investigated and, allowing for the incubation period, certain suspects are picked out. The feces and urine of the suspected contacts are examined once. This examination may detect a carrier who can then be further investigated. If this examination is negative, a Widal reaction should be made, if possible, and anyone with a positive reaction should be reexamined by the duodenal tube method. Any suspects with a positive or doubtful history should also have a reëxamination of duodenal contents. Some one of these examinations will usually give positive results.

In routine surveys, the feces and urine of all individuals should be examined once. History of the disease should be inquired into and those with a positive or doubtful history should be reëxamined by the duodenal tube method.

SPECIMENS

Feces. Loose stools are more favorable for positive results as the bacilli are brought down from the duodenum more rapidly. Calomel has the reputation of being a good cathartic for carrier specimens. Dried bile is also used. Individual specimens are easily obtained by providing the patient with a labelled container and directing them to use a chamber. A convenient form of container is a glass vial with a metal scoop fastened to the cork. A pill box of tin or card board with a tongue depressor for collection may also be used. All containers should have a blank paper label for identification of the specimen. If the specimen cannot be examined within a few hours, the vial should contain a mixture of 30 per cent glycerin in salt solution which keeps the typhoid group of organisms alive for a longer time. One part of feces should be mixed with about two parts of solution.

For collecting large numbers of specimens more organization is necessary. The most certain method is to take the specimen direct from the rectum. A cotton swab is put into a piece of glass tubing about 10 mm. in diameter, the end of the tube is vaselined and gently forced through the anus. The swab is then pushed into the rectum, rotated and withdrawn and put in a sterile tube or in the glycerine solution mentioned above. The swab alone can be used, if the cotton is firmly attached and the buttocks are well separated. Care must be used not to break off the end of the swab in the rectum. An enema tube can also be used to advantage as fecal contents collect in the opening. Otherwise wooden or paper plates or pieces of wood can be used to receive the movement and, after the specimen is taken, these can be buried or burned.

Urine. Urine should be collected in a small sterile bottle. A catheterized specimen is not necessary for diagnosis. Some observers recommend a specimen from a mixed twenty-four hour collection. Positive urine is often cloudy and very rich in bacilli.

Duodenal contents. This specimen can be obtained with less difficulty than might be expected. An Einhorn tube, or modification, is used (fig. 6). The procedure should be carried out on a nearly empty stomach and duodenum. The early morning is

a favourable time, after a light breakfast. The patient sits up on a bed or couch. The metallic tip is chilled and then swallowed while the operator gives moral support. The patient should then lie down on right side with knees drawn up and rest as the tube gradually descends. Usually one to two hours are required. Some workers give the tube in the evening and make the examina-

Fig. 6. Picture of Duodenal Tube

A convenient variety of the Einhorn Duodenal Tube, some form of which is essential in efficient typhoid carrier work.

tion in the morning. This long procedure has never been necessary in my hands. A flow of fluid should be established by syphonage or by slight suction with a syringe. The first fluid is, of course, stomach contents. A test of reaction should be made with litmus or better with methyl red and phenol red (0.02 per cent

watery solution). The former is red in an acid medium and yellow in an alkaline one. With phenol red the colors are reversed. As soon as a change occurs in the color or consistence of the flow, a fresh container should be used to receive the material and another test of reaction should be made. Usually when the duodenum has been reached a yellow syrupy fluid appears which reacts yellow with methyl red and red with phenol red. This specimen is then examined in the laboratory. Naturally, if acid gastric juice is submitted for examination, no information of value will be obtained. While the tube is still in place, the Lyon technique can be carried out, which consists in pouring into the tube, through a small funnel, about 30 cc. of a 25 per cent solution of magnesium sulphate. Syphonage is then reëstablished and frequently a darker colored fluid or "B" bile is obtained. If this is really gall bladder bile, it would be preferable to plain duodenal contents, but as duodenal contents are usually satisfactory and there is doubt about the origin of B bile, this procedure for carrier work is an unnecessary refinement.

TECHNIQUE

The duodenal contents are spread directly on Endo plates. Some of the specimen should also be incubated for twenty-four hours and other plates inoculated. A microscopic examination of the centrifuged sediment may show leucocytes in positive cases. The further procedure is given below.

A drop of liquid feces or a mixture of hard feces in broth is spread on the surface of differential media and search made for colonies characteristic of the typhoid group. Only by experience can the proper amount of inoculum be judged. It is best to use several plates and the usual trouble is too many rather than too few colonies. Some workers enrich specimens with dilutions of brilliant green. This method succeeds at times, but fails at others. If the time which the bacteriologist might devote to enrichment were spent in securing specimens of duodenal contents, the end results would be much better. Many differential media have been proposed, such as lactose litmus agar, eosin methylene blue agar, malachite green, phenol red or brom cresol purple media. All have their merits and drawbacks. In the Army Medical School

method, worked out by Russell, Endo medium is used and in spite of some drawbacks, is most serviceable. As it rapidly deteriorates, the ingredients are kept separately—3 per cent extract agar, pH 7.8, is kept in flasks and sterile solutions are prepared of 10 per cent lactose, saturated alcoholic solution of basic fuchsin and 10 per cent watery sodium sulphite. A few hours before use, the agar is melted, and the ingredients are added—1 per cent lactose, 1.8 cc. fuchsin and about 25 cc. sulphite to the liter. The agar should then be cooled to about 50° and poured into Petri dishes, small or large. The agar is allowed to harden with the cover ajar in a dust free place. The specimen is then spread with a loop or a right angle glass spreader. Incubate twenty-four hours and examine for colorless, translucent, non-lactose fermenting colonies. Mark and transfer several to Russell double sugar tubes, inoculating both butt and slant (3 per cent agar with 1 per cent lactose, 0.1 per cent glucose, pH 7.6 and phenol red as an indicator). If the colonies are numerous enough, agglutination can be done immediately with colonies made up of small Gram negative bacilli.

The double sugar tubes are incubated for twenty-four hours and are then examined for characteristic appearance of the typhoid group. This for the typhoid bacillus is an acid butt with no gas bubbles and an alkaline slant. With Para A or B, the butt is acid and broken up with gas bubbles and the slant is alkaline, especially so with Para B. Colon bacilli produce more gas in the butt and an acid slant, which, however, may turn alkaline in case of B. aerogenes.

Growth from typical double sugar tubes are stained and if Gram negative bacilli are found, agglutination is done with specific sera by transferring a suspension or a loopful to different dilutions of serum. If satisfactory agglutination and controls result, the diagnosis is made. The culture should be plated out and a pure culture kept for reference or confirmation.

The urine is plated direct in liberal quantity and also incubated in about five parts of broth and plated again after twenty-four hours. The growth of bacilli in carriers is often rich and pure. Occasionally excretion is periodic.

As soon as the bacteriological diagnosis is made a further clinical diagnosis of the location of the focus is necessary. This involves examination of specimens from the duodenal contents if not already made and cultures after ureteral catheterization in case of urinary carriers. A diagnosis of biliary passage lesion can be made if the duodenal contents are positive, but whether the focus is confined to the gall bladder or whether it also occurs in the liver cannot be told, except as a result of operation. An X-ray picture may assist in locating the lesion in a urinary carrier, as it is usually a unilateral pyelitis.

A diagnosis of the kind of carrier should also be made, whether convalescent or contact, based on the history and probabilities of slight illness. The epidemiological significance of the carrier should also be looked into, such as history of occurrence of previous cases among his contacts, and so forth.

TREATMENT

After a thorough diagnosis is made, further spread of bacilli should be prevented as far as possible by insisting on good personal hygiene of the carrier. If the carrier will not observe rules or is an old offender, quarantine may be enforced with legal sanction in many places. Under these circumstances the carrier is more apt to agree to radical treatment.

In the technical treatment, surgical measures are the most effective. The focus in many carriers is a single local one which can be cured by excision. Thus many carriers have been cured by cholecystectomy and nephrectomy. Unfortunately, in some cases the foci are multiple, especially in the biliary tract and excision of one focus does not cure the condition. Such carriers can be determined only by operation and are incurable at present, but probably form the minority. Cholecystectomy should, therefore, be tried in all cases possible. Cholecystectomy with hepatic drainage has been advised for liver carriers. Illustrative specimens are given in figures 7, 8, and 9.

The technical details of the operation cannot be discussed here, but the situation calls for coöperation on part of the surgeon. The diagnosis, made by the internist or pathologist, must be accepted without clinical evidence. Especial effort should be

made not to damage the individual. In convalescent cases, operation should not be performed until at least six months after recovery, as some cases will spontaneously clear up during this interval.

FIG. 7. GALL BLADDER AND GALL STONE FROM A TYPHOID CARRIER REMOVED AT OPERATION SEVEN YEARS AFTER ORIGINAL ATTACK

Carrier was a member of the Army Nurse Corps. Operation cured the carrier condition. (Reprinted with permission from Journal of the American Medical Association.)

Many other methods of treatment have been tried and some partial success apparently has been obtained, but the results are so irregular, compared with those of surgical treatment, that coincidence may explain them. (See Chapter IV.)

FIG. 8. GALL BLADDER AND GALL STONES FROM A TYPHOID CARRIER REMOVED AT OPERATION SEVEN YEARS AFTER ORIGINAL ATTACK

Carrier was an army cook who was detected by routine examination of food handlers. Operation did not cure the carrier state.

FIG. 9. DRAWING OF HALF OF LEFT KIDNEY REMOVED FROM URINARY TYPHOID CARRIER SIX YEARS AFTER ATTACK

Carrier was an army cook who was detected by routine examination of food handlers. Pyonephrosis in which a pure culture of typhoid bacillus was found. Cure by operation. (Reprinted with permission from Journal of the American Medical Association.)

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CHAPTER VI

Cholera

Next to the discovery of the cholera vibrio in the intestinal tract of patients, the recognition of a chronic cholecystitis as a focus of the carrier state was the most important advance in the possibilities of control of this disease. The carrier conception was first reached in the study of cholera, but the practical consequences of this discovery were not generally realized until a pathological basis for the existence of carriers was established. Cholera in endemic centers occurs with distant seasonal regularity. There are intervals of complete freedom from the disease. The whereabouts of the vibrio in this interval was a mystery until a chronic cholecystitis was recognized. Much ingenuity was expended on possible life cycles in the environment, but, as is frequently the case in the infectious diseases, the trouble was found closer home. The carrier is now believed to be the real reservoir of the disease from year to year. While the acute case causes most other cases during an epidemic, the carrier causes the epidemic itself. The carrier problem in cholera is most difficult in endemic centers as the natives have racial and religious prejudices and personal habits which are foreign to scientific medicine. On the other hand, where bacteriological examinations and quarantine can be enforced, as in the case of emigrants, it has been shown by the Public Health Service that wholesale carrier work is possible and is effective in protecting the country from cholera. Most of the recent work in the prevention of cholera in India (Grieg) and in the Philippines (McLaughlin, Munson) has been along carrier lines.

Incubationary carriers are known who pass vibrios in the stools for days or weeks and finally develop the disease. Digestive upsets from irritating food or catharsis may precipitate the attack. Such cases can be distinguished from contact carriers only by the outcome, as no test of immunity is available.

As in the case of typhoid, the number of organisms in the body become rapidly reduced in most cases within the time of clinical

recovery. A small number, about 3 per cent, do, however, become convalescent carriers and reservoirs of infection. These carriers are apparently not as persistent as typhoid carriers, but final statements can not be made on this subject until more work is done on cultures of duodenal contents in life and on gall bladder contents at operation and autopsy.

Contact carriers are still more temporary. They may be as numerous as 6 to 30 per cent. Care is necessary to rule out mild infections.

PATHOLOGY

As in the case of faecal typhoid carriers, a focus is found in the gall bladder. This consists of a mild catarrhal inflammation which gives no clinical symptoms and is discovered only by inference after bacteriological examination or at autopsy. It is not known whether lesions occur in other parts of the biliary system. Although the subject has not been as fully worked out as in typhoid carriers, the high percentage of positive findings in the bile strongly suggest that the cholecystitis is the principal carrier focus.

There is no general agreement as to the pathogenesis of this lesion. Some observers favor the theory of ascending infection through the common duct, others (Greig), infection through the lymphatics. Cholera vibrios do not invade the blood to the same extent as typhoid bacilli, but they are not confined as strictly to the intestinal tract as was once thought, because they have been found in the urine during life and in the lungs at autopsy. A theory of portal system septicaemia with excretion of the vibrios through the bile has been advanced by the author to account for the cholecystitis. In any case, the lesion occurs and lasts for an indefinite time. Further work along these lines is much needed. An experimental cholecystitis can be reproduced experimentally in rabbits and especially in guinea pigs by intravenous injection or direct inoculation (Schöbl).

Carrier strains of the vibrio have been studied from the comparative point of view and no differences have been noted as compared with strains from cases. Atypical strains, however, are especially apt to be troublesome. They may not agglutinate and their significance remains uncertain.

DIAGNOSIS

The same general rules apply as in typhoid carriers. The final diagnosis is bacteriological, but the personal history and epidemiological circumstances may assist in the detection. Sero-agglutination may also be of value in some instances.

Cultures of duodenal contents of suspected carriers have apparently not yet been made on any scale, but the information which can be gained in this way would be very valuable from many points of view.

The specimens of feces are collected in the same way as in typhoid carrier work. As large numbers of persons must often be examined in a short time, an organization of the work is necessary.

TECHNIQUE

The principle of diagnosis is to isolate a vibrio which agglutinates with a specific serum. The special points, in the isolation, are the use of enrichment and a selective medium which favors the development of the vibrio and inhibits other organisms. A rectal swab or small amount of feces is enriched in alkaline peptone water, pH 8.4, for several hours. A transfer from the surface is then made to a second tube. After six hours the surface growth is spread on alkaline agar, pH 8.4 (faintly alkaline to phenolphthalein). This medium allows a good growth of the vibrios in translucent colonies. Material from the suspicious colonies is stained with dilute carbol fuchsin and examined for vibrios. If present, a micro-agglutination is made with standard anti-cholera serum, or a transfer is made to alkaline agar and a macro-agglutination is made the next day. If the reaction is clear cut, a diagnosis can be made. A transfer of the culture should be saved for confirmation. Some typical vibrios do not agglutinate well at first. Further cultural and serological work is necessary. There are many unsettled problems of strains of vibrios which apply to carrier as well as clinical work. No reliable virulence test is available.

A great many differential and special media have been devised for cholera work. In general, the simplest is the best, and the above outline will give good results.

When carriers have been found, an effort should be made by the history and by further examinations to classify the carrier and to determine the social bearings of the condition.

TREATMENT

The first measure is isolation and instruction in personal hygiene. Intestinal upsets should be avoided as they may precipitate an attack in an incubationary carrier. Many carriers are relatively of short duration and will clear up while under observation. For chronic carriers, as in typhoid, many measures have been tried, but with irregular results. In long term chronic carriers, surgical measures should be considered.

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CHAPTER VII

The Dysenteries

A. BACILLARY DYSENTERY

The carrier is apparently of less importance in the spread of dysentery than in the spread of typhoid or cholera. There are fewer true carriers and the individual carrier is less chronic and excretes fewer bacilli. Acute and chronic cases are usually responsible for spreading infection. On the other hand, definite instances are recorded of spread of this serious disease through apparently healthy carriers.

Incubationary carriers are known. In the absence of a test for susceptibility and in view of the relapsing character of the attack, it is difficult to diagnose such carriers except by careful consideration of the previous history and subsequent course.

In temporary convalescent carriers, the curve representing the presence of bacilli in the feces falls gradually after clinical recovery, but does not reach a low percentage for about two months. Repeated examinations are necessary to exclude the carrier state.

Chronic convalescent carriers, running up to a year, occur in 1 to 5 per cent in different series. It is difficult to draw the line between relapsing carriers and chronic cases. Flexner bacillus infections are more apt to result in carriers, while Shiga bacillus infections are more apt to be chronic cases.

Contact carriers have usually been considered as rare, but with improvement in technique of examination, are found more frequently. Here again the exact diagnosis is difficult between a convalescent carrier after a mild case and a true contact carrier who has never been sick.

Pathology

In the true contact carrier the bacilli apparently have no focus and live for a short time in the lumen of the colon.

In the convalescent carrier the lesion is an ulcer of the original attack which has failed to heal with the establishment of a general immunity. The ulcers of bacillary dysentery have characteristic differences from amoebic ulcers. They usually run transversely, are superficial and occur in the ileum as well as the caecum. Dysentery bacilli apparently do not regularly invade the blood and other foci, as in the gall bladder, are rare. Urinary carriers are unknown.

Diagnosis

The personal history of intestinal trouble and of residence in infected regions may be suggestive. The presence of mucous in the stool is suspicious. Epidemiological data are also often useful.

In the laboratory diagnosis, the finding of the organism is of course the main object, but examination of the blood serum for agglutination may be of much assistance and sometimes a presumptive diagnosis must be made on agglutination alone. The agglutination curve usually falls promptly after convalescence and its persistence in strength up to 1–50, or 1–100 is very suspicious, especially in view of the difficulties of stool examination.

Technique

The general rules given for the examination of feces of suspected typhoid carriers apply here. Examination of the rectum with a protoscope sometimes reveals an ulcer which can be cultured directly. In the stool mucous should be sought for and plated on several plates. A great many media have been used. Lactose litmus agar is one of the simplest and best. Endo medium should be used, but is not favourable for the growth of the Shiga bacillus.

The plates after incubation are examined for non-lactose fermenting colonies and transfers are made to Russell double or triple sugar in the regular way. The reactions in the Russell tube are identical with those of typhoid bacillus. There is an acid butt with no bubbles of gas and an alkaline slant. If typical growths in the tubes show on staining a Gram negative bacillus, agglutination is done with monovalent sera at a strength corresponding to the titre. There are a number of organisms whose significance in actual dysentery is uncertain and the same is true

in carrier work. If an organism is isolated it should be agglutinated with the individual's serum for additional data. A negative reaction would tend to rule out a convalescent carrier, but not a contact carrier. At least three release cultures should be made over two or three weeks as the bacilli are hard to find.

Treatment

The field of specific treatment with serum vaccines has not been thoroughly explored, but is not promising. If the ulcer is in the rectum alone local treatment is effective. Usually the most that can be done is general hygienic treatment with lavage of the colon. Instruction in personal hygiene should be given. Continued observation is necessary.

Medical Research Committee. London, Special Reports Nos. 7 and 40.

B. PROTOZOAL DYSENTERIES

1. Amoebic dysentery

The pathogenic amoeba, Endamoeba histolytica, is not limited to the tropics as closely as was formerly thought and amoebic dysentery, or more properly amoebiasis, is a serious cause of ill health in many parts of the world. Amoebiasis is the better term as dysenteric symptoms may be slight or absent and the principal damage may be anemia, neurasthenia, or liver abscess. In the spread of this infection carriers play an important part. In fact, the cyst, which is the only infecting stage in the life cycle of the amoeba, is characteristic of carriers rather than of cases, as its presence indicates that a balance is being reached. The vegetative forms, which produce the symptoms, are not infective. From the point of view of the parasite, therefore, the transmission of the disease is due to a carrier stage in 100 per cent of instances. In the acute stages of the infection, cysts are not found as frequently as in the chronic stages. It may be difficult at times to differentiate a chronic case from a true carrier, as cases merge into carriers and carriers into relapsing cases; but true carriers do exist, with a limited active focus and many cysts. The immunity in such protozoal diseases is not as clear cut as in bacterial diseases. A balance is more easily reached and with less evidence of infection.

The percentage of temporary convalescent carriers is very high. On the Mexican border in 1916–1917, Craig found that of 115 cases, 86, or about 75 per cent, developed cysts and became at least temporary convalescent carriers. The further history of such carriers is not entirely known. Spontaneous cure of some cases and carriers undoubtedly occurs, but even with the best treatment about 10 per cent may remain carriers. The percentage of so-called contact carriers is said to be much more numerous than convalescent carriers, but the possibility of a mild or atypical attack is to be kept in mind. In the general population, carriers are of course most prevalent in endemic centers in the tropics and least in temperate regions. Thus, Young, in Manáos, Brazil, found no less than 27.5 per cent of native troops, apparently in good health, harboring cysts of Endamoeba histolytica, whereas among army recruits in England, Mathews and Smith found only 5.6 per cent carriers. The possibilities of carrier infection through food handled by careless and ignorant native servants have often been realized.

Pathology. In the chronic convalescent carrier the lesion is an unhealed ulcer of the colon. Here the vegetative forms of the parasite persist and produce cysts. This cyst cannot reproduce itself and the vegetative form cannot live long in the intestinal contents. It requires some focus or home in the intestinal wall. Hence, the pure contact carrier is very temporary. So-called chronic contact carriers are either mild chronic cases or convalescent carriers from mild infections.

Chronic foci occur in other parts of the body, as abscesses, but usually have no natural outlet. One case of gall bladder lesion has come to the writer's notice. The patient, a medical officer, had an enlarged gall bladder and incidentally was an amoebic carrier. The gall bladder on removal had a thick leathery wall. The contents were purulent and showed many active amoebae. Amoebae were also found later in the wall by section. Soon after operation he was free from the carrier state. This condition is possibly not as unusual as it seems.

Diagnosis. This is made by the microscope. No serological reactions are available. Clinical history and circumstances may be suggestive. A formed stool is preferable for looking for cysts.

Frequently a diagnosis can be made with the fresh specimen by finding of four nucleated round or oval cysts. In general, however, on account of the frequent presence of other cysts in the feces, it is preferable to have stained specimens examined by an experienced worker. Differentiation must be made from cysts of the harmless amoeba and those of other protozoa. Occasionally material can be obtained directly from a rectal ulcer. A single examination will detect only about one-third of carriers.

In the examination of large numbers of individuals, which must be made if the carrier program is to yield results, some organization is necessary. Specimens must be properly collected, labelled, and so forth, as was emphasized under discussion of specimens for typhoid carriers.

Treatment. The treatment is that for the original infection and must be directed both against the vegetative forms in the tissue and the cysts in the feces. Emetin is best for the tissue infection. Hypodermic injections in courses are given of $\frac{1}{3}$ to 1 grain a day for seven days with a short rest and repetition. Toxic symptoms must be watched for such as neuritis, especially of the legs, and myocarditis. The cysts in the feces can be reduced by large doses of bismuth subnitrate, one heaping teaspoonful in one-half glass of water before meals. Emetin bismuth iodide by mouth has advantages in both directions, but it is apt to nauseate. Courses of 3 grains daily for twelve days cured 91 per cent of cases in the English experience. Colon lavage with quinine 1:1000, or argyrol is of value.

Repeated negative examinations are necessary for release as single examinations are inadequate.

Carriers should be instructed in personal hygiene and kept in quarantine if not too numerous. If the number is too large for quarantine, personal hygiene and sanitation must be depended on.

2. Other protozoal dysenteries

True carriers are definitely known in one other form of protozoal dysentery, namely, Balantidiosis. The disease is comparatively rare. The carrier relationships are much the same as in amoebiasis. The vegetative forms live in ulcers in the wall of the

intestine and form cysts which are excreted and are infective. It is possible that the vegetative forms can live some time in the feces and encyst there. If this is so, true contact carriers would have more of a place than in amoebic dysentery. The pig, a common scavenger in the tropics, is infected with a similar parasite.

Emetine and arsphenamine should be tried in treatment.

Besides these true carriers, there are a large number of possible carriers of other protozoa, such as trichomonads, lamblia, et cetera, whose clinical significance is not yet well understood. They may be primarily pathogenic in some cases, or they may be purely secondary or saphrophytic. Giardia intestinalis is generally regarded as pathogenic, but there is considerable doubt about the importance of other protozoa. The carriers of most of them are probable pseudo carriers.

In all these conditions, with the possible exception of trichomonas infections, the cyst stage of the parasite occurs as the basis of a possible carrier state.

In Giardia infections, it is often difficult to differentiate a case from a carrier as the symptoms in a case may be mild and indefinite. The lesion is in the duodenum where the parasites become attached to the mucous membrane. True carriers are either immune or slightly infected.

The diagnosis is made on the absence of definite symptoms and the finding of cysts in the intestinal contents. The duodenal tube has been used to good advantage as motile forms have been found in duodenal contents when the feces were negative or showed only a few cysts.

The diagnosis of carriers of intestinal protozoa requires considerable experience and technique. A large number of cysts or cyst-like bodies occur in feces and frequent errors in interpretation have been made which vitiate many diagnoses and sets of statistics.

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CHAPTER VIII

Helminthoses

Carriers of helminths are recognized and play a definite part in the spread of diseases due to worms. They are not dangerous to their immediate contacts, like the intestinal carriers so far considered, as the parasites must develop outside the body before infection is possible. The carrier, therefore, infects only his environment and is most important in warm parts of the earth where the population lives close to the soil.

In these infections it may be especially difficult to distinguish between cases and carriers. A person may become immunized to the effect of the parasite and thus be a true carrier, but usually a carrier is one who has not enough parasites to be a case. Thus, in hookworm infections, the number of worms necessary to produce any real disease is put at 10 to 100 or more by different authors. A person with a few worms would thus be a carrier. While from the theoretical standpoint it is very desirable to have well defined standards of cases and carriers, it is a mistake, from the practical point of view, to split hairs over the diagnosis.

While carriers usually infect their environment less than cases, a continued small infection will in time be as bad as a single massive infection.

Carriers in hookworm infections will be described as typical of this group because this infection is best known and other less well known diseases seem to be similar in general.

Carriers are very prevalent in infected regions. A large percentage of persons excrete ova but only a few will show symptoms. Hence, the carrier is a real problem.

PATHOLOGY

The carrier lesion is the same as the case lesion. The worms attach themselves to the mucous membrane of the ileum and feed on bits of tissues and tissue juices. Their number is so small, however, that they do no general damage. They may live for a time free in the lumen like other round worms.

DIAGNOSIS

Residence in an endemic area is suggestive and history of exposure to skin infection or of ground itch may be obtained. Examination of blood for eosinophilia may also be suggestive. The final diagnosis depends on finding ova or worms in the stool.

It has been found that the number of ova in the stool is roughly an index of the number of worms present. If we, therefore, adopt as a standard of carrier state, 10 to 100 worms, the condition can be diagnosed by less than one ovum per 100 fields.

The diagnosis may be made by direct examination of the stool, but concentration methods are much better on account of the scarcity of ova. The brine method of Barbour was found most useful for examination of large numbers of men during the war. The feces were mixed with equal parts of a hypertonic salt solution in a small container such as a salt cellar or pill box and allowed to stand a few minutes. The eggs float to the top and will attach themselves to the under side of a slide placed over the surface.

TREATMENT

This is the same as for a mild infection. Carriers can be cured by a course of thymol, oil of chenopodium or carbon tetrachloride. If possible, the stool should be strained and worms counted. Subsequent examination will tell results of treatment.

In general management, carriers must be considered in same class with cases, and feces should be disposed of so that soil will not be infected. As the cure is so easy, no hardships on the individual are necessary.

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CHAPTER IX

Diphtheria

It is generally accepted that diphtheria is largely kept in existence by chronic carriers who act as reservoirs and furnish the bacilli at favorable seasons to susceptible individuals. If it were not for carriers the disease would be much less of a problem. On the theoretical side the control of carriers has been carried nearly to a stage of perfection. The possible carrier can be diagnosed with comparative ease. The virulence of the suspected organism can be determined with considerable certainty. The susceptibility of possible hosts can also be determined and the treatment of the carrier is fairly effective. Hence, theoretically we are in a very favorable position to stamp out this disease along carrier lines. Practically, however, the program usually breaks down because it is too big. The number of exposed and susceptible persons is usually large. The laboratory and clinical facilities are usually limited. Only a certain number of cultures can be examined in a day and only a much smaller number of virulence tests can be made. Only a certain number of Schick tests can be made and several days' observation are needed. Only a certain number of persons can be quarantined or held under observation. The result is that the purely bacteriological line of attack fails and common sense governs as it should. Clinical cases are considered first and as much carrier work is done as is feasible. As laboratory facilities increase, more is accomplished along these lines, but it is doubtful if carrier work alone can be sufficiently well done to produce a radical effect on the prevalence of diphtheria. The most promising results are being obtained by a combination of case work, carrier work and active immunization of Schick positive children. The toxin antitoxin treatment seems to give a high and lasting immunity and the most practical objective is to produce a large number of immunes along with a reduction of the foci of infection. The immunization program is not sufficient alone as the reactions among adults are too severe for general practice.

However, the fear of producing a large number of carriers among immunized children is groundless, as these contact carriers are temporary. The worst carriers are the chronic convalescent ones.

Incubationary carriers. These carriers can be recognized and play some part in the dissemination of bacilli, but the incubation period is so short and the diagnosis of a virulent organism in a Schick positive individual requires so much time that the incubationary carrier cannot be assigned a very definite place in carrier work. If they are found, however, they should be treated like cases.

Convalescent carriers. With convalescence the bacilli begin gradually to disappear and, by the end of a month, 85 per cent of convalescents are bacteriological recoveries. By the end of a second month, 98 per cent are free. The remainder pass into the most dangerous class of more or less chronic carriers. Foreign bodies or deformities in the nose and throat predispose to the chronic carrier state. Release cultures made during early convalescence are examined only morphologically. Virulence tests are not necessary as it has been found (Wadsworth) that 90 per cent of strains from convalescent carriers are virulent up to three months after recovery.

Contact carriers. Pure contact carriers occur among attendants, families and contacts of cases and carriers in from 10 to 20 per cent of instances. The organisms are virulent in 80 per cent of instances, and the carriers are dangerous, but the condition is temporary unless there is some predisposing deformity of a chronic focus. These carriers are immune or Schick negative.

In the general population true carriers of virulent organisms are less than 1 in 1000. Among children, however, 2 per cent are true carriers. Only 10 per cent of non contact or non convalescent carriers show virulent organisms.

Possible and pseudo carriers. In any extensive carrier work a number of individuals will be found who are carrying organisms which morphologically resemble true virulent diphtheria bacilli. A preliminary tentative diagnosis must be made pending further examination. Virulence and cultural tests show that many of these organisms are diphtheroids or non-virulent diphtheria bacilli. The final diagnosis should be made of pseudo carrier and

the individual should be released from observation. No long term quarantine should be carried out, as has been done, on morphological grounds alone.

PATHOLOGY

The focus in incubationary carriers is at the site of the coming lesion, usually in the throat near the tonsils and consists in the first stages of invasion. The number of organisms is probably large.

In the contact carrier there is either no lesion or a nonspecific one due to some other cause such as a foreign body or a deformity on which the bacilli become engrafted. The lesion then comes to resemble that of a convalescent carrier.

Chronic convalescent carriers. The tonsil is most frequently the focus in the chronic convalescent carrier and may be taken as typical. Other similar foci may exist in the adenoids or sinuses, but the tonsil is most frequently and longest infected. The crypts have a local diphtheritic inflammation of their walls. The lining epithelium is disintegrated and replaced by inflammatory tissue which pours out an exudate into the crypt and on the surface of the tonsil (fig. 1). There is a characteristic fibrinous exudate in the lesion. The diphtheria bacilli are easily found in sections and are clearly out of reach of surface disinfection (fig. 10). These carriers have a general but not a local immunity. The general immunity may be carried over from the disease or it may be constantly produced by the small carrier lesion which acts as a vaccination.

DIAGNOSIS

Suspected diagnosis may be made on epidemiological or clinical grounds, and a clean tonsillectomy is evidence against the carrier state, but the final diagnosis is bacteriological and the presumptive laboratory diagnosis is relatively so simple that wholesale cultures are usually made without regard to clinical or epidemiological probabilities. If Schick tests have previously been made on any of the suspects, the results should be obtained.

The specimen. A sterile swab should be pressed on each tonsil and passed over the faucial entrance. Repeated examinations in-

crease the percentage of positive results. Nasal specimens obtained by passing separate swabs through each side of the nose to the nasopharynx, also reveal additional carriers. Nasal obstruction may interfere with free passage of the swab, but may be the

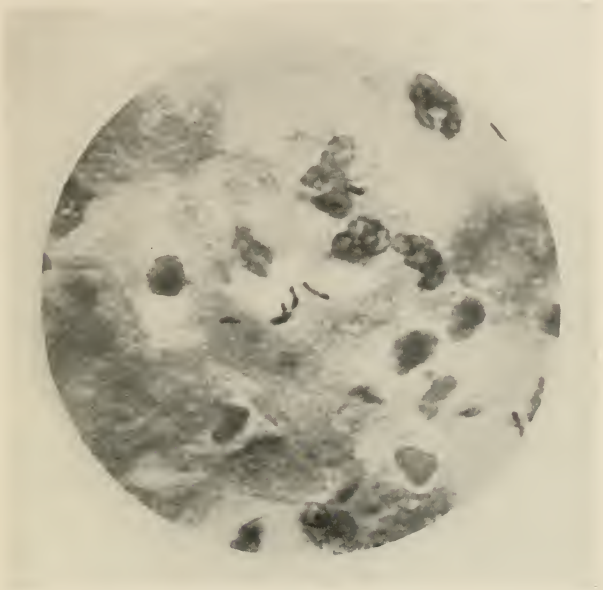

FIG. 10. DIPHTHERIA BACILLI IN TONSIL OF A CONVALESCENT CARRIER THREE MONTHS AFTER ATTACK. HIGHER MAGNIFICATION OF PREVIOUS PHOTOGRAPH (FIG. 1). × 1000

Diphtheria bacilli in the walls of the crypts. Bacilli cultivated from this tonsil were virulent for guinea pig.

predisposing cause of the infection. The swab should be immediately passed over the surface of coagulated blood serum in a tube or box or plate and incubated, or the swab be sent to the laboratory and inoculated there. The organisms resist drying and low

temperature, but speed is an object. Direct smears from the throat are not as useful in the diagnosis of carriers as they are in some cases.

While the culture is incubating Schick tests should be started, if possible, by the intracutaneous injection of 0.2 cc. of $\frac{1}{50}$ M.L.D. of toxin for a guinea pig of 250 grams with a control of toxin heated to 75° for five minutes.

Usually the incubation is carried on for over night but shorter incubation gives positive results in some cases. Incubation for 48 hours is said to increase positive results by about 10 per cent. Smears are made from suspicious colonies or from the mass growth and are stained by alkaline methylene blue, Gram's or Neisser's stain. The presumptive diagnosis is made on morphological grounds. No special morphology of carrier strains is recognized. Doubtful findings should be checked by further specimens and more detailed examination. Meanwhile possible carriers should be quarantined. If the carrier is an early convalescent or contact carrier, a virulence test is not necessary as most of these strains are virulent. But if the carrier state is long continued or of doubtful origin, virulence tests must be made.

TECHNIQUE

It is of course most satisfactory to isolate the organism in pure culture, but in view of the large number of cultures to be tested a rough test may be more serviceable. The slant from which the diagnosis was made is washed off in 2 cc. NaCL and 1 cc. injected subcutaneously in a guinea pig. If the pig does not die in three days it may be concluded that the culture is avirulent. If the pig dies with characteristic injection oedema of the site of inoculation and with hyperaemia of the adrenals it may be concluded that the culture is virulent. Too often, however, the pig dies with indefinite evidences and it can not be decided whether the animal died of diphtheria intoxication or mixed infection.

A pure culture is obtained by emulsifying material from the original tube in broth and spreading a loopful well over a blood agar plate. Loeffler plates may be used, but are more troublesome to make and are not much superior. Single suspected colonies are fished and stained and if positive morphologically are trans-

ferred to broth or to a Loeffler or blood agar slant. After forty-eight hours 1 cc. of the broth culture of a virulent organism should kill a pig in three days. If the slant is used it is washed off and one-half is given. As a control, a guinea pig may be injected with the same dose and immunized with 500 units of antitoxin, but ordinarily this is not necessary. It is more economical to use the intracutaneous method by which a number of tests can be made on the same animal, but more experience and skill are necessary.

When a carrier is found an attempt should be made by regional cultures to locate the focus. Usually both tonsils are infected but the infection may be in one or in one side of the nose.

There are now several possibilities. The patient may have a virulent organism and a negative Schick test—he is a true carrier, contact or convalescent. The history may decide which. He may have a non-virulent organism and a negative Schick test; he is a pseudo carrier. He may have a virulent organism and a positive Schick test; he may be an incubationary carrier or early case and should have antitoxin. He may have an avirulent organism and a positive Schick test, he is a psuedo carrier, but toxin antitoxin treatment should be considered.

As was said before, in trying to handle large numbers of cases, as in schools or troops, this ideal scheme usually breaks down and common sense rules, that is, cases are given priority and carriers are considered if possible.

TREATMENT

Many carriers clear up by themselves in time. Release cultures should be continued. For the resistant cases, many lines of treatment have been proposed, but excision of the focus by tonsillectomy is the most effective except in the rare cases when the lesion is elsewhere. On the specific side, antitoxin does not affect the bacteria. An antibacterial serum has been made and used as powder for use by insufflation. Cures have been reported, but cures have also followed the use of powdered meningococcus serum. The effect is probably a non-specific inflammatory reaction. Insufflation of kaolin also acts in the same way. Attempts have been made to implant lactic acid bacilli and staphylococci. The former is ineffective, the latter dangerous. Every sort of

antiseptic has been proposed. The most reasonable are silver nitrate, 10 per cent, and iodine, 2 per cent in glycerin. If these antiseptics are applied actually to crypts they may succeed in some cases; but this procedure requires more care than is usually available and the crypts have underground communications. It is simpler and more effective to remove the tonsil. This operation however, should not be done until several months after the disease in order to avoid the complication of endocarditis.

X-ray treatment of the tonsil has been proposed and is preferable in some cases. Several treatments are necessary. The action is to shrink up the lymphatic tissue and improve nutrition and drainage. There is no antiseptic effect.

In cases which resist tonsillectomy, correction of other foci possibly in sinuses and irrigation of nose and throat with saline is indicated.

Isolation. Carriers of virulent bacilli should be isolated. Appropriate treatment for the kind of carrier should be carried out. For release, three successive negative cultures should be required at daily intervals without any local treatment. No protracted isolation should be imposed unless the organisms are proved to be virulent.

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CHAPTER X

Epidemic Meningitis (Meningococcus Infection)

Next to diphtheria carriers, carriers in meningitis have the most definite place among the respiratory diseases. The experiences of the war brought the carrier aspects of the disease especially into prominence. It is probably more exact to speak of meningococcus infections than of meningitis, because apparently there may be a local infection in the nasopharynx and a blood infection without true meningitis. The carrier is recognized as an essential part in the continued existence of the disease. The case is generally too sick to spread the germs extensively, while the carrier is free to do so. On the other hand, the radical control of the disease by carrier work alone is generally considered impossible on account of technical and administrative difficulties. Our insufficient knowledge of virulence and immunity also weakens a radical carrier attack. English experience has also apparently shown that increasing the air space is usually effective in controlling the disease among troops. Carrier work, therefore, tends to be confined to convalescents and immediate contacts and is combined with other general measures.

The object of the carrier program is of course to prevent a virulent organism from reaching a susceptible individual. In the problem of the meningococcus infection, we have no simple clinical method of determining either the virulence of the meningococcus or the susceptibility of the host. Such bacteriological and clinical work as has been done on the subject indicate the following situation (Heist). Strains from the throats of carriers are not as virulent as strains from the spinal fluid of cases. Some carrier strains are more virulent than others. Not over 5 per cent of persons are susceptible to carrier strains. The results seem to throw some light on the epidemiology of meningitis and may explain the difference between the seriousness of the case and the relative harmlessness of the carrier.

Incubationary carriers exist and constitute about 0.5 per cent of all carriers. Convalescent carriers number up to 5 per cent for

three months after convalescence and occasionally much longer. Contact carriers are more temporary, but more numerous. Some surveys made during the war ran very high with but very few cases. In the general population the percentage is about 3. As we have no simple test for virulence and immunity, the only logical carrier method of attack would be to examine all concerned and to isolate those carrying either of the two recognized types of meningococci. The amount of technical and administrative work involved usually defeats such a plan.

Special mention should be made of one feat during the war in which the entire 89th Division of 40,000 men were cultured for carriers. This was done under the direction of Lieutenant-Colonel E. H. Schorer at Camp Funston, Kansas. The Division Surgeon was Colonel J. L. Shepard, M.C., U. S. A. The men came from an endemic area of meningitis and in spite of the ordinary measures, cases continued to appear. It was decided to examine the entire division for carriers and this was accomplished in about six weeks, by using six officers as swabbers and nine officers in the laboratory while the enlisted men worked in day and night shifts. About 3 per cent of carriers were found. Altogether during the winter of 1917–1918, 102,170 cultures were made and 3290 carriers were detected and removed from their organizations. Meningitis ceased to be a problem when the work was accomplished. The results have been criticized on the ground that such mass work is too crude technically. Some evidence on this point is seen in the fact that out of a total of 152 cases of meningitis, 16, or over 10 per cent occurred in incubationary carriers who had been already detected by the survey. The removal of these men alone diminished the exposure rate by 17 per cent.

At the outbreak of the war, the expert advisors recommended general carrier work. When the technical difficulties of applying these measures on a large scale were realized, carrier work became limited to convalescents and immediate contacts. But the work at Funston showed that success in phorology depends largely on the energy and determination of the individuals concerned rather than on the official program. If the laboratory facilities are or can be made adequate and if the circumstances are sufficiently urgent, carrier work should be more and more extensive.

PATHOLOGY

Comparative regional cultures show that the principal carrier focus is in the vault of the nasopharynx. No conclusive pathological studies of the lesion are available. It is usually believed that the meningococci live superficially in the crypts of the mucous glands. A large amount of mucus is thought by many observers to indicate the carrier possibility. But in some instances the meningococci inhabit the epithelial barrier without marked disturbance. Predisposing conditions are found in other lesions, especially deformities of the nose and lymphoid overgrowths. Some carriers show meningismus with a normal spinal fluid.

DIAGNOSIS

The diagnosis can sometimes be suspected on clinical and epidemiological grounds from the personal history and evidence of nasopharyngeal trouble. Skin tests with bacterial powder or solutions have not been specific enough to pick out carriers. The agglutination test is occasionally valuable.

The bacteriological diagnosis requires special care in securing and handling of the specimen, as the organisms lie in a protected position and are especially fragile.

A good nasal swab is sufficient, the more elaborate West swab being unnecessary. The most open side of the nose should be entered and the swab pushed to the back wall of the nasopharynx, then rotated and withdrawn.

The specimen should be kept warm and moist until the media is inoculated. The media must also be kept warm after inoculation. The English in the war devised special warm containers to carry specimens in. Whole or laked blood media is most convenient, but any serum enriched medium can be used. The specimen is planted first on a small surface at the edge of the plate, then with a sterile loop the plate is streaked radially. Schorer put several cultures on the same plate. After incubation, typical colonies are picked and stained and Gram negative cocci are selected for further work. They are transferred to other media for macro-agglutination or in some instances may be agglutinated microscopically with polyvalent and normal and para

type sera. No diagnosis of a true carrier should be made except with type identification.

The following extracts are made from the Standard Technique of Meningococcus Carrier Detection issued by the Medical Departments of the Army, Navy and Public Health Services during the War: These directions were prepared by a committee of specialists whose chairman was Col. F. F. Russell, in charge of the Division of Infectious Diseases and Laboratories of the Surgeon-General's Office, U. S. Army.

I. Culturing.
   a. Wherever possible the cultures should be taken in a small room in the regimental infirmary. The floor of this room should be washed with an abundance of soap and water one hour before the men enter for culture, and should be wet during the process of culturing.
   b. Only *a few men* at a time should be admitted to the culture room.
   c. Windows and doors should be closed all the time.
   d. Cultures should not be made within an hour after meals.
   e. No men should be examined on the same day on which they are sprayed.

II. Method of Swabbing.
   a. The swab used should be:
      1. A naked wire 25 cm. long, with a small absorbent cotton pledget on one end, well covering the end of the wire, and a ring handle on the other. The wire should be flexible, such as stove pipe wire or hay baling wire, of about 18 gauge. The swabs may be sterilized in glass or paper containers in groups of 5–20. The last 1 to 2 cm. of the pledget end of the swab is bent to an angle of about 30 to 40 degrees. This swab is simple and has proved most satisfactory, and can be at once discarded.
      2. West Tube. This gives satisfactory cultures, but is cumbersome, and not strictly necessary.
      3. Straight unprotected nasal swab. This is useful in the case of individuals with highly irritable throats, but is not recommended as a routine.
   b. The subject should be seated facing the light. Tongue depressors are to be used when necessary. The swab should be passed behind the soft palate while the subject is phonating. The swab, having passed up behind the palate, is introduced successively into each posterior naris, and then is drawn across the posterior wall of the naso-pharynx.

The swab is then withdrawn, taking care not to touch the throat surfaces or the tongue; this is best accomplished during phonation. The success of carrier search depends largely on the care with which the swabbing is done, hence the man taking the cultures should be able to execute these directions skilfully. He should be either a nose and throat specialist, the bacteriologist himself, or directly under the latter's supervision.

III. Method of Inoculating Plates.

a. The mucous charged swab should be applied over a limited area at the periphery of the plate. From this the spread is made by a wire loop passed by a series of radial strokes, each starting from the infected point. If there is very little mucus it is often possible to smear directly from the end of the swab.

b. A single person per 10 cm. plate is preferable. More than two cultures on one plate should never be made.

c. The plate must be inoculated while warm and kept warm until replaced in the incubator. To accomplish this, sterile plates already warmed by storage in the incubator, should be packed in a device insulated against the loss of heat, such as a fireless cooker, for transportation.

Care should be taken to keep the plates warm during the inoculation process. It is advisable to carry a plate seeded with known culture of meningococcus to act as control.

IV. Culture Medium.

a. Standard nutrient 2 per cent agar. (Beef infusion, or Liebig's beef extract, 0.5 per cent NaCl, 1 per cent peptone, Fairchild's or Difco; reaction; plus 0.5, phenolphthalein.) Dextrose is not necessary. A convenient method of storage is in 200 to 300 cc. quantities, in flasks of sufficient size to permit of the addition and mixing of the following:

1. Defibrinated blood—human, horse, sheep, goat, or rabbit —about 1 to 10 cc. of agar.
2. Laked blood. (Blood, 1 part; distilled water, 3 parts; of this mixture add 1 to 10 cc. of agar.) Both these blood preparations should be stored ready for use in the ice box. They are good as long as they remain uncontaminated, and the whole blood unhaemolysed. They should be added to the agar only when the latter is at a temperature of 45° to 50°C.

b. Starch agar is suitable for stock cultures, and for mailing cultures.

c. Plates should be incubated, inverted, over night before use, to insure sterility.

V. Examination of Inoculated Plates.

a. Plates should be inverted when placed in the incubator.

b. Plates will be ready for examination after twelve to eighteen hours' incubation at 37.5°C.

c. Discard all plates that are crowded and do not show discreet well separated colonies.

d. The meningococcus colony on the whole blood medium does not produce green coloration or haemolysis. It tends to be somewhat larger than the streptococcus and pneumococcus. The colonies are moist, elevated, outlines are ill defined, and on moderately opaque blood agar have a faintly bluish tint. The colonies are not usually opaque, a characteristic which distinguishes them from the staphylococcus.

On transparent blood medium and with transmitted light under lens magnification the colony may be nearly clear, but often shows a very faint smoky gray-blue quality. This characteristic is intensified by passing the finger between the light and the colony to shade it. Further lens effect may be seen by moving the plate so that the colony passes across some distant obstruction to the light as a string stretched across the window. The colony is never granular, in young cultures.

The colony should be confirmed by smear and Gram stain.

VI. Transplantation.

The suspected (ringed) colonies are transferred to warmed moist blood agar slants. They must have been incubated to insure sterility. It is best to keep the tubes continuously in a warm water bath until finally placed in the incubator. If transfers are made under these conditions there will be enough growth for identification in about eight hours.

Two essentials to success in growing meningococci are moist media, kept constantly from the time of inoculation at body temperature.

VII. Identification.

a. Microscopic. Smear preparations are made in the usual way stained by Gram. The presence of a few gram positive, or other contaminating organisms does not make the culture unsuitable for agglutination.

b. Agglutination. All Gram negative micrococci are subjected to agglutination in the following way:

The serum dilutions are first set up, and the bacterial emulsion is made directly in them. To make this emulsion a loopful of the suspected culture is scraped off, and the loaded wire is passed well down the tube almost to the level of the fluid. The bacterial mass is then rubbed off against the

wall of the tube and mixed with the fluid. In the case of the meningococcus a smooth emulsion is usually rapidly produced. Many of the other organisms are much less readily emulsified.

An emulsion must be free of clumps for proper agglutination tests.

The quantity in each tube should be 1 cc. The tubes are then incubated at 55° for twelve to eighteen hours, with necessary precautions against evaporation.

Controls. Each culture should be run in parallel with a normal horse serum control at 1:50. A known meningococcus culture should be run at a positive control with each set.

VIII. Reading of Agglutinations.

The tubes which have been clarified are then shaken gently when the clumps can be clearly detected by the naked eye or hand lens.

The organisms which are agglutinated by the polyvalent serum dilutions at 1:100 are to be regarded as meningococci.

Organisms which agglutinate in both polyvalent and normal horse sera are to be thrown out.

A slight opalescence in the supernatant fluid due to contaminating organisms, if there is otherwise distinct evidence of alggutination, need not lead to the discard of the culture as negative.

IX. Typing.

The meningococcus isolated by agglutination with polyvalent serum should be typed as soon as possible. If this procedure cannot be carried out on the spot, the cultures, or heated suspensions of the cultures in saline with 0.5 per cent phenol, should be sent to the nearest Department Laboratory.

XI. Typing of Organisms.

Organisms recovered from spinal fluid or blood should be typed and compared with the organism isolated from the patient's nasopharynx.

Inagglutinate strains are sometimes encountered. To establish further the nature of these organisms they should be grown on dextrose, maltose, and saccharose serum-litmus-agar.

XII. Indications for Culturing.

On the appearance of a case of cerebro-spinal fever, all contacts should be cultured for the detection of carriers as soon as possible. By contact is meant those intimately associated with the patient—that is, all those in the same tent or squad room with him, as well as his close associates at mess or elsewhere.

Experience has shown the inadvisability of attempting to culture larger groups than this.

In military service, those who give positive cultures should be held in the detention camp until they have had three successive negative cultures at five-day intervals. If a second case appears in the same company within a week of the first case, the whole organization should be swabbed.

XIII. Disposal of Carriers.

The ordinary carrier usually clears up in a week or two.

Those who carry longer than this constitute the chronic carriers, and usually give large numbers of colonies or even pure cultures; these are probably the important cases from a public health point of view.

Such carriers should not be recommended for furlough to their homes, nor discharged from the service without authority from the Surgeon General.

TREATMENT

Fortunately most carriers are temporary and the problem is relatively easy. They should be isolated and given the best of hygiene, especially out-of-door life. Correction of deformities including tonsillectomy may be necessary.

Many antiseptics were tried during the war without definite success. In some instances the condition was made worse.

Specific measures, vaccination or serum treatment, have no definite place in treating carriers.

The handling of carriers in large numbers requires hospitalization and quarantine. The plan usually collapses. During the war carrier camps were maintained where regular work was done.

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CHAPTER XI

Pneumococcus Pneumonia

Contrary to the usual historical sequence, carriers, of some sort at least, were discovered before cases in pneumococcus pneumonia. Both Sternberg and Pasteur, in 1890, demonstrated the presence of pathogenic micrococci in the saliva of healthy individuals before the possible relation of these organisms to pneumonia was established. Even when these organisms were recognized as pneumococci, there was little or no advance in epidemiology because it was believed that pneumococci were homogeneous. Only within the last few years, since the recognition of types of pneumococci, has come the possibility of intelligent epidemiological and carrier work. It is now realized that the true carrier is a factor which cannot be disregarded.

Before the differentiation of types, it was taught that pneumococcus pneumonia was largely autogenous and depended on a lowering of resistance. It is still true that this kind of pneumonia occurs, especially following influenza, but at least two-thirds of the cases of pure lobar pneumonia are caused, not by the kind of pneumococcus present in the mouths of normal persons, Type IV, but by Types I and II. These are the epidemic strains. They are not found ordinarily in the mouth except in convalescent or contact carriers.

Type IV, or more exactly Group IV, occurs in 20 to 50 per cent of normal mouths. It produces about one-fifth of the total number of cases, especially the secondary ones. It really stands for a collection of types which cannot be recognized and handled as such. Hence, Group IV carriers do not figure in the program. Type III and atypical Type II pneumococci stand between Group IV and Type I and Type II pneumococci. They are definite types but also occur normally in the mouth. The Type I and Type II carriers are the only ones which have a definite place in carrier work at present. The subject is a difficult one technically and the recent prevalence of influenza has confused the situation by the increase of other

kinds of pneumonia. However, there is no doubt that the pneumococcus Type I and II are primary causes of disease (Cecil and Blake) and that the carrier relations prevail. In view of the technical difficulties of typing and of our known lack of control, the radical handling of the pneumonia problem by the carrier method is out of the question. Tests of virulence and susceptibility are also not yet available as practical measures. Something, however, can be done with convalescent carriers and immediate contact type carriers. The general situation must be handled by general hygienic measures, by isolation of cases and carriers and by specific vaccination.

Convalescent carriers of Type I and II pneumococcus are definitely known, as about 40 per cent of Type I and II convalescents have the type organism in their saliva. These are usually temporary, existing about a month, but may last longer. Contact carriers are also well recognized, having been found in over 10 per cent of the Rockefeller Hospital series. They are also temporary, lasting about a month. The writer made a study of pneumonia in a large camp in 1916 and found evidences of squad, company and regimental type epidemics. Fifteen per cent of tent contacts of Type I cases were found to be temporary, contact carriers. No incubationary carriers were detected.

PATHOLOGY

No special carrier lesion is recognized for pneumococci. As most carriers are temporary it is probable that no special lesion exists. The pneumococci, apparently, live for a short time on the mucous membrane of the mouth like the more saphrophytic types. The tonsil, of course, is a favourable soil, but type carrier foci have not been definitely located there. There may be semichronic lesions in the lungs or bronchi, but they have not been identified.

DIAGNOSIS

The history of a recent attack of pneumonia or of contact with the disease raises the possibility, but the type of the previous attack or contact is often unknown. Bacteriological diagnosis must be depended on; serological reactions are not definite enough.

The technique is more difficult than in a case as the organisms are fewer and more mixed with others. A faucial swab or saliva can be plated on blood agar and suspected colonies fished to glucose broth for tests, but it is better to use the mouse method by injecting 0.5 cc. of mixed saliva into the peritoneum. Sometimes the peritoneal exudate can be used directly for typing as in cases, but often it is too much contaminated and cultures of heart blood or subcultures of peritoneal exudate must be made. The usual staining, agglutination and bile solubility tests must be made and sometimes be supplemented by cultural reactions. Occasionally two types may be found, as I and IV. Usually only one saphrophytic type is present in the mouth.

TREATMENT

Cases should be isolated as far as possible and contact should be limited. Convalescent type carriers should be kept isolated for a reasonable time or until two or three negative cultures are obtained. Contact carriers should be warned of possible danger to themselves and others. They should be kept in good condition and avoid contaminating others. Usually they clear up in a short time. On analogy the nose and throat should be looked after for local predisposing lesions. No data are available on the results of the use of antiseptics.

Laboratory facilities usually are too limited for any extensive general carrier work, but they should be used for this purpose as far as possible.

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CHAPTER XII

Streptococcus Infections

Historically, the best known carriers of streptococci were the surgeons and students of the premicrobic period, who after treating cases of puerperal fever or making post mortem examinations, infected puerperal women by local examination. These were mechanical contact carriers who do not belong to the present age.

The most important streptococcus carriers of today are those involved in the streptococcus diseases of the respiratory tract, such as tonsillitis, pharyngitis, rhinitis, sinusitis, otitis media, mastoiditis, bronchitis, pneumonia and empyema. The experiences of the war and of the influenza pandemic emphasized the seriousness of this group of diseases and much work has been done especially on the carrier relationships of streptococcus hemolyticus. It has been established that carriers exist and play a part in the spread of the organisms. Methods of treatment are also effective. The part played by carriers in the production of the disease is not so clear. The principal drawback is that we have no ready means of picking out true carriers from among possible and pseudo carriers. The large scale on which any measures must be carried out is also a complication. Finally there is uncertainty as to the primary or secondary importance of the streptococci. Hence, the rôle of carriers is still obscure. Radical control by carrier measures is not possible but the indications are to push the carrier program as far as conditions permit.

There are of course other streptococci than the hemolytic types in the respiratory tract and in some cases the differentiation of feeble hemolyzers is not simple. Among individuals infected with these other streptococci, possible carriers exist. If the current views of the etiology of endocarditis and other forms of focal infection are correct, undoubtedly some virulent strains of streptococcus viridans are carried by certain individuals. At present, however, these true carriers cannot be picked out and attention must be confined to carriers of hemolytic streptococci.

Some workers claim that by repeated cultures hemolytic streptococci can be found in 100 per cent of throats. It is certainly true that a single culture gives no adequate picture of the ultimate bacterial flora of the throat, and that successive cultures increase the percentage of positive findings. The conclusion should not be drawn, however, that all hemolytic streptococci found in the throat are normal inhabitants. All the evidence points to the probability that there are different groups of streptococci and that there are true carriers. During the war surveys showed that recruits freshly arrived, especially from rural districts, had a relatively small percentage of positive findings, about 5 per cent, which soon increased to equal the high rates of those who had been longer in crowded camps, 50 to 80 per cent. These surveys were mostly made on single cultures and more thorough work might have raised the percentage, but could hardly have obliterated the striking difference. The number of carriers usually detected by ordinary examination is 10 to 20 per cent.

In considering the question of groups of streptococci, it is fairly well settled that there is a distinct scarlet fever streptococcus. This differentiation has been made on immune reactions and confirmed by several different workers and is so clear cut that the question of the streptococcal origin of scarlet fever is again open. The further grouping of hemolytic streptococci is not so definite. Some workers (Dochez and Avery) have made four groups on immunity reactions, while another worker (Gordon) has made only one. The sugar reactions in all the groups are generally the same (Holman), but there is a distinct group of mannite fermenters (streptococcus infrequens). Virulence tests might be of great value but it is difficult to standardize a test and virulence falls off rapidly on subculture. Havens and Taylor have recently done some work in this line. They injected into the peritoneum of a mouse, one-fifth of a twenty-four-hour growth of the first blood-agar-slant-transfer from the original blood agar plate. Death in twenty-four hours was taken as the standard of virulence. They found that only 10 to 15 per cent of strains from carriers were virulent while of strains from acute respiratory cases about 85 per cent were virulent. Virulence diminishes rapidly after an attack of tonsillitis, for example, but,

as the authors point out, it is impossible to assume that these organisms might not be or become virulent for a non-immune.

Group carriers. The only way to approach the subject is to regard carriers of streptococcus pyogenes and streptococcus infrequens (Holman) as possible carriers. Walker and Norton have shown that the infrequens group can be studied as a unit clinically and epidemiologically. As virulence and susceptibility are better understood, it will be possible to concentrate on the true carriers. The carrier is probably dangerous to himself as well as to others. In other words, relapsing carriers exist who suffer clinically when their immunity decreases.

PATHOLOGY

The most definite carrier lesion is found in the tonsil. Other foci may exist in the adenoids, turbinates and gums but the tonsil is the richest and most persistent source of the organisms. The lesion consists of an actual infection of the crypt wall. The epithelial lining is disintegrated and infiltrated with polynuclear leucocytes (fig. 11). Streptococci are also found in the crypt contents, especially in the actinomyces-like granules (Davis).

The typical lesion is found in chronic convalescent carriers. Hypertrophied tonsils are most apt to be positive. Eighty per cent of such removed tonsils give a positive culture. In contact carriers the streptococci probably also lodge in the tonsil. It is impossible to state the exact pathogenesis in these carriers. The carrier is probably temporarily immune to his own organism, but repeated attacks of tonsillitis are of course the rule.

DIAGNOSIS

The presence of hypertrophied tonsils in young individuals is suggestive. Persons with clean tonsillectomies are rarely carriers or if so, carry few organisms. The actual diagnosis is bacteriological. The specimen should consist of crypt contents and is obtained by pressing the ordinary throat swab on the tonsil or going into the crypts with a loop. Occasionally the lesion is unilateral. Well spread smears are made on 5 per cent blood agar plates and after twenty-four hours incubation, hemolyzing colonies are examined by staining for Gram positive cocci in chains. The

hemolytic influenza bacillus and hemolytic staphylococcus must be ruled out. A presumptive diagnosis can often be made on clear cut hemolysis in the original plate and speed is an object when cases are being held for the results of cultures. Frequently

FIG. 11. DRAWING OF SECTION OF TONSIL OF A STREPTOCOCCUS HAEMOLYTICUS CARRIER. × 1000

Streptococci are shown in the disintegrated epithelial covering

the hemolysis is not clear cut. The colony must be subcultured into broth and a hemolysis test made with 0.5 cc. of twenty-four hour broth culture and 0.5 cc. of a 5 per cent suspension of red cells. Even with this test some results are partial and doubtful. Such organisms are usually regarded as non-hemolytic. Further

subdivision is made by sugar reactions, on lactose, mannite and salicin. Inulin and bile solubility tests are used to exclude pneumococci. Immunological classification of carrier strains is not on a practical basis. Virulence tests are also not standardized.

TREATMENT

As in diphtheria carriers, many attempts have been made to cure streptococcus carriers by the local application of antiseptics. The results have been disappointing. If the streptococci were simply growing on the surface of the crypt walls and if the crypts were all accessible, this line of treatment would be more effective. But the streptococci are often actually in the wall of the crypts and the crypts have underground connections which cannot be reached except by dissection. The most effective antiseptic in securing negative cultures is 25 per cent silver nitrate, but streptococci can still be cultivated from the depths of the crypts after soaking an excised tonsil in a 25 per cent silver nitrate solution.

The surest method of treating carriers is tonsillectomy. Most cases clear up immediately after the operation. In some instances a few streptococci can be found after clean tonsillectomies, but the danger of transmission is of course greatly reduced with the number of organisms. The operation should not be done until a month or two after an acute attack, in order to avoid systemic infection. The operation must also be a complete one as a small tag of tissue may be a carrier focus.

X-ray and radium treatment have been proposed as a substitute for tonsillectomy and in selected cases, in which there is a contraindication to operation, should be tried. Undoubtedly some tonsils contract considerably under this treatment and the number of organisms become smaller. But the large hypertrophied tonsils are less suitable than the boggy ones for X-ray treatment. Several treatments are also required and while there may be clinical improvement, in many instances the streptococci persist. This result is of course a failure from the social point of view.

Probably only in isolated instances will an operation be done simply for the carrier state. This state, however, is an additional argument for the operation when coupled with clinical indications.

The following recommendations were made at a symposium on this subject in 1919:

I. Our knowledge of hemolytic streptococcus carriers is so incomplete that every effort should be made to answer the following questions:

a. Are streptococci found in carriers all of equal importance, or are there different groups which differ in clinical significance?

b. Is the chronic carrier dangerous to himself?

c. Is the chronic carrier dangerous to others, or is the disease spread chiefly by cases or by case contact carriers?

II. In the absence of knowledge on these points, no final program for handling the problem can be stated, but a tentative program should be adopted which in case of doubt should err on the safe side.

III. When no streptococcus disease is present and in off seasons.

A. For soldiers in hospital. Incoming patients with throat infections should be cultured for hemolytic streptococci. Any positive case with diseased tonsils should have a tonsillectomy. Clean and infected measles wards should be maintained for practice in ward technic.

B. For soldiers in barracks. Clinical and cultural surveys should be made for the detection of chronic streptococcus infections such as tonsillitis and otitis media, which when discovered should be treated to remove possible foci of future epidemics.

IV. In the presence of streptococcus complications and during the streptococcus season.

A. In the hospital.

1. No carriers among attendants should be allowed in surgical wards or in wards with respiratory diseases.

2. A streptococcus isolation ward should be established to handle special cases.

3. Positive and negative measles, pneumonia and nose and throat wards should be maintained with strict technic.

4. All admissions should be isolated until distributed to wards.

5. Throat cultures for hemolytic streptococci should be made on all admissions with respiratory diseases for record.

B. In barracks.

1. Recruits should be held for observation and cultured. Positive cases should be separated from negative as far as possible.

2. Clinical and cultural surveys should be made to pick out cases of tonsillitis, otitis media, sore throat which should be sent to hospital.

V. In the absence of exact knowledge and with due regard to military necessity, no attempt to isolate all streptococcus carriers is advocated at present.

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CHAPTER XIII

Other Respiratory Infections

By analogy the carrier aspects of the large group of diseases known as colds, influenza, etc., are undoubtedly important, but little practical headway can be made along carrier lines on account of the uncertainty as to the etiology of these diseases. Many different organisms have been put forward as causes, but none is fully accepted as a primary factor. The possibility of a primary filterable virus must be disposed of before any advance is made. As Metchnikoff says, this possibility is a "sort of ghost preventing all definite conclusions in problems connected with the absence or presence of microbes." On grounds of epidemiology and analogy there are probably incubationary carriers, convalescent carriers, either temporary or chronic, and contact carriers. But as long as the parasite is unknown, nothing can be done along carrier lines except to isolate cases early and continue the isolation for a reasonable time. There is no better illustration in medicine for the necessity of scientific knowledge as a basis for practical work. Our good intentions and organizations are helpless without it.

INFLUENZA

The influenza bacillus is the principal storm center in this discussion. It has been found in 100 per cent of cases of influenza by combined cultures and animal inoculations. It has also been found in about 30 per cent of convalescents. On the other hand, it has been found in about 20 per cent of normal non-contact individuals. The value of any set of statistics can not be determined until there is an answer to the following questions: Is any form of the influenza bacillus the primary cause of influenza? Are there groups of the organism, epidemic and saphrophytic? What part is played by changes in virulence? Until we have more definite knowledge on these points, no practical carrier work can be done.

Irrespective of its relationship to influenza, the influenza bacillus is recognized as a pathogene, especially in meningitis in children. There is some evidence of the existence of a special meningitis group of organisms (Rivers). The hemolytic influenza bacillus is usually regarded as non-pathogenic.

Pathology

The sinuses, especially the sphenoids, are foci for the influenza bacillus (Hopkins and Robertson). At autopsy a purulent exudate with a pure culture is frequently found. The working out of the significance of the lesions depends on the outcome of the work on the problem of etiology.

Diagnosis

The diagnosis is a purely bacteriological one. The more specimens from different parts of the respiratory tract examined, the higher are the positive results. Usual throat swabs are inoculated on chocolate agar and colonies made up of Gram negative bacilli are transferred to blood agar and plain agar. The results of these cultures indicate whether the organism is hemoglobinophilic or hemolytic. Further test may be made for indol production (Jordan) which separates 40 to 50 per cent of influenza bacilli from Koch-Weeks bacilli. Toxicity tests and grouping at present are not available.

Treatment

In view of the uncertainties mentioned above, no radical carrier procedures are justified. Cases should be confined to bed in isolation for a reasonable time.

VINCENT'S ANGINA

This condition shares with others in uncertainties of carrier work. It is disabling and at times is undoubtedly epidemic. During the war the disease was quite prevalent in the form of "trench mouth." In attempting to handle the situation along rational lines we are again confronted with a wilderness of confusion. The organisms of Vincent's angina may be accepted as causal but they occur, at least in small numbers, in normal mouths

in a very high percentage of individuals. They are practically normal inhabitants. On the other hand, apparently some strains are virulent and produce ulcers and spread to others. How are the two organisms related to each other and to the disease? Are they primary or secondary causes? If primary, how can the epidemic strains be identified? There is no adequate answer at present to these crucial questions. Hence no scientific basis exists for carrier work.

During the war some enthusiastic medical officers, especially dental officers, tried to enforce the carrier program by isolating all cases until negative release examinations were obtained. Contacts were quarantined on the mere presence of a few fusiform bacilli and spirochetes in smears. These measures threatened to entirely tie up the activities of one camp and were ordered discontinued on the basis that our knowledge does not justify such a radical program. The situation must be handled by treatment, hygiene and sanitation rather than carrier work at present.

TUBERCULOSIS

The term carrier is sometimes used in tuberculosis to indicate an apparently healthy person who discharges tubercle bacilli. Such true convalescent carriers may exist who have a general immunity with a small unhealed lesion somewhere in the body. But, in general, such individuals should be considered as mild or chronic cases. In view of the nature of the disease and of its mode of spread, more good will be done to the individual and to the group by emphasizing cases rather than carriers.

On the other hand, if the term is accepted, there are a large number of true relapsing carriers. As infection apparently occurs in childhood and clinical cases later in life are due to an autogenous spread from a chronic glandular focus, we may say that relapsing carriers are of the greatest importance in this disease. The danger is primarily individual and secondarily social. One organ becomes the unit and the individual represents a group of organs. According to this analysis, the relapsing carrier comes under the definition of a carrier, as an individual who harbors and transmits a pathogenic parasite, only as the parasite is transmitted from one organ to another. This extension of the carrier conception is perhaps undesirable; but, even from the practical point of view,

a consideration of the importance, pathology, diagnosis and treatment of relapsing carriers as seen in latent and focal infections is instructive.

DISEASES OF UNKNOWN ETIOLOGY OR DUE TO FILTERABLE VIRUSES

There is a formidable list of so-called respiratory diseases in which little practical carrier work can be done as the cause is unknown or, if known, requires such a special technique for identification that it cannot be handled clinically or in a public health sense. This list includes measles, scarlet fever, mumps, smallpox, chicken pox, poliomyelitis, encephalitis and possibly influenza and colds (Foster).

Work on poliomyelitis has been most instructive in this group and gives a rational basis for at least some carrier measures. The possibility of carrier transmission was opened up by epidemiological studies before experimental confirmation occurred. After the virus was identified, it has been shown by animal inoculation (1) that incubationary carriers exist (Taylor and Amoss); (2) that convalescent carriers exist, occasionally lasting seven months; (3) that contact carriers occur which probably out-number cases and play as important a rôle as a meningococcus carrier; (4) that the tonsils are foci in carriers.

Considering the experimental difficulties involved in this work, it must be clear that even the few observations on which these statements depend have thrown much light on the problems of prevention of this disease and the entire group. While it is usually impossible to do individual carrier work at present on account of the lack of laboratory facilities, some general rules can be laid down. Cases should be isolated at the earliest possible moment. Logically the same rule should apply to any indefinite sickness in childhood, but is usually out of the question. Convalescents should also be isolated for about three weeks. Contacts, if they occur, should be under suspicion. The tonsils are again shown to be a menace and the hygiene of the nose and throat is emphasized.

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CHAPTER XIV

Blood Diseases

This group might also be called the insect transmission group as the parasites live largely in the blood vessels and exit is usually provided only by puncture of a blood vessel.

MALARIA

Carriers play a well known part in the continued existence of malaria. As in amoebiasis, there are special forms of the parasite, called gametes, whose function it is to perpetuate the life of the parasite in the insect host. The vegetative forms which produce the symptoms are not infective for the mosquito, but in about 50 per cent of cases, gametes are found and convalescent or relapsing carriers result. The gametes are more numerous in the chronic than in the acute stages of the infection. Hence all the circumstances are favorable for the infection of the mosquito by the carrier.

In malarious regions gametes are found in the blood of about 10 per cent of apparently healthy adults. In children the percentage may be much higher. Strictly speaking, all carriers in malaria belong to the convalescent carrier group either as chronic convalescent or relapsing carriers. An infection of the red cells by the vegetative forms is necessary before the sexual stages can develop. Hence, the true contact carrier does not exist. Practically speaking, however, such carriers do exist in the sense that they have never been conscious of their original infection.

Pathology

Carriers in malaria are particularly instructive from the point of view of immunity. There is a true infection but a balanced parasitism which is apparently reached by an antitoxic without an anti-parasitical immunity. A special focus exists in the capillaries of the spleen, liver and brain. The balance is delicate and toxic symptoms or frank relapse may occur.

Diagnosis

Previous residence in malarial regions is suggestive. Clinical examination may show an enlargement of the spleen. In the laboratory examination an increase of mononuclear leucocytes is suggestive. The actual finding of the parasite is more difficult than in cases, as the parasites are fewer and the gamete must be identified. In aestivo-autumnal infections, however, the gamete has a characteristic crescent shape which is distinctive. It has been estimated (Darling) that a certain percentage of gametes per mm. of blood is necessary for infection of the mosquito and, therefore, to constitute a carrier. Usually an ordinary blood film is made and stained by a polychrome method. The thick film method is valuable in experienced hands. Cultural methods (Bass) are difficult technically and reveal only the vegetative forms. Various drugs have been suggested to bring the parasites into the peripheral circulation such as ergot and adrenalin. Ultra violet light has also been used to produce relapses.

Treatment

The prompt treatment of an acute case with quinine prevents the development of gametes and hence prevents carriers. After the infection is established the treatment of carriers must be more prolonged, as the gametes are not affected by quinine. The formation of new gametes can be prevented however, and the old forms gradually disappear from the blood. Intravenous therapy is no more effective than alimentary. In carriers who do not tolerate quinine, arsphenamine should be used.

OTHER DISEASES OF THE BLOOD

The most important other infectious diseases of the blood are relapsing fever, yellow fever, trypanosomiasis, filariasis, bubonic plague and typhus. Human carriers are not known in yellow fever, plague or typhus. If they occur, the parasite probably leaves the body by some other avenue than the puncture of a blood vessel by an insect.

Trypanosomiasis is so progressive and fatal a disease that true carriers do not occur in the human host. In the animal host, carriers are considered in a later section.

Filariasis is a true carrier disease in the sense that the infected individual often shows no evidences of disease. The commonest variety of infection is due to Filaria Bancrofti. This disease is of most importance among native races in the tropics, but there is a focus in Charleston, South Carolina, and white men are occasionally infected in the tropics. Probably the infection occurs principally in early life. The distribution is often sharply localized. Carriers of microfilaria may run from 5 to 20 per cent in an endemic area as in certain islands in the Philippines, while in other islands the rate is much lower.

Pathology

The mother worm is so situated in the lymphatics that no symptoms arise. Sometimes there are internal evidences of disease with none externally.

Diagnosis

Residence in an endemic area is suggestive. Examination of night blood shows the characteristic periodicity of parasites in the peripheral circulation. The parasite can also be found by examination of a large amount of day blood.

Treatment

No active treatment is effective at present. Carriers should be protected from mosquito bites to prevent spread. They can be disregarded otherwise.

SKIN DISEASES

The skin is of course infected by various bacteria, fungi, blastomycetes, spirochetes, protozoa and metazoa and definite carrier aspects of some of these infections occur. It is not considered worth while, however, to enlarge on this subject in this manual at present. The lesions are usually so noticeable and so accessible for local treatment that possible carrier lesions are usually regarded as mild or chronic cases.

CHAPTER XV

Sexual Diseases

1. syphilis

As in tuberculosis, it may be questioned whether it is correct to speak of carriers in syphilis rather than of latent cases. The infection is so apt to be slowly progressive that this criticism has some point. But, unlike tuberculosis, syphilis is usually spread by a form of contact which has special carrier aspects. It also has such a direct although insidious effect on the welfare of the race that an exception should be made, if necessary, to emphasize the social menace of the situation. The prospective bridegroom, infected but apparently healthy, is really carrying spirochetes which will disable his wife and blight his offspring. It is splitting hairs at the expense of public health not to recognize that the apparently well syphilitic is a great danger in the organized social relations of marriage. For practical purposes, therefore, cases of latent syphilitic infection, especially males, may be considered carriers. They have all the characteristics of apparent health combined with the most malign possibilities for harm that other carriers present. The female infects only through an open active lesion or occasionally as a mechanical carrier.

The number of latent male cases is somewhat problematical as it depends on the whole number of cases which is variously estimated by different workers. If we assume, as we can on good grounds, that 10 per cent of adult males at any one time have syphilis and that 50 per cent of these are in a latent stage, then there would be over 1,000,000 such carriers in the United States at present. They can be classed as chronic convalescent carriers as they have recovered from the acute generalized stage of the disease and have reached the stage of localization, or they can be considered as relapsing carriers.

Pathology

The carrier lesion is in the testicle in the great majority of carriers. There are many other foci of spirochetes in the blood vessel walls of other organs and in the nervous system, but these have no natural outlet. The lesions have been most carefully studied by Warthin by the combined method of ordinary histology and of sections stained for the organism. They consist of small, often microscopic, collections of lymphocytes among which are nests of spirochetes. In the testicles these foci communicate with the tubules and the organisms are discharged with the semen.

The seriousness of the situation consists in the fact that the spirochetes are genitotropic. Experimental work has shown that the testicles are the most favorable place for their growth and that they lodge there by preference. Their distribution elsewhere in the body may be determined partly by chance, but they will certainly lodge in the testicle in the great majority of cases. The carrier is temporarily immune to the toxic effects of the parasite, but not locally immune to the parasite itself. A balanced parasitism is reached as in other carriers.

Diagnosis

Illness of the sexual partner, miscarriage and stillbirths are suggestive. A truthful personal history with clinical examination may be almost conclusive, as the presence of a primary scar with adenopathy and the history of previous treatment is very suspicious. Very often, however, the carrier is truly unaware of his condition. The original attack has been mild and unnoticed. For exact diagnosis, a confirmed completely positive Wassermann reaction, done by a competent serologist and in the absence of certain rare diseases, is conclusive evidence of syphilis. This test, taken with the results of clinical examination, are usually convincing. Weak reactions and indefinite clinical signs of course occur and make it necessary to balance probabilities. A provocative Wassermann is sometimes valuable. Examination of the spinal fluid is justified in doubtful cases as nervous system involvement is probably second to that of the generative organs.

The diagnosis by the demonstration of the spirochetes in the seminal fluid has been made both by direct examination and by animal inoculation. The specimen can be obtained by use of a condom or by massage of seminal vesicles. Examination by the dark field microscope or by injection into rabbits' testicles have given positive results in apparently well individuals who were candidates for marriage. These procedures, however, belong more to research than to clinical medicine. The virulence of the parasite apparently decreases somewhat as the disease progresses, but both experimental inoculation and clinical experience show that the virulence remains for years high enough to infect.

Treatment

This is the usual one for the disease—the chronic combined treatment with arsphenamine and mercury. In general the author believes that optimism as to results is justified. Standards of cure are not entirely agreed upon; but a carrier should not be considered safe for marriage until he has had definite treatment and a negative serological and clinical year has elapsed with no treatment. Mechanical protection against direct contact can of course be used.

2. GONORRHOEA

True carriers exist in gonorrhoea, both in males and in females, and are responsible for a good share of the trouble caused by the gonococcus. The principal bad effects are blindness in children, sterility and chronic ill health in women, stricture, prostatitis and arthritis in men. The line between a chronic case and a carrier can be drawn by giving sufficient attention to history and examination. Most carriers are of the convalescent type. The percentage of complete cures is not very large. The pure contact carrier may apparently occur in the prostitute. She may be a primary or secondary contact carrier and may transmit the organisms mechanically from a case or carrier to the new case.

Pathology

Small inflammatory or ulcerative lesions persist in the urethra, prostate, seminal vesicles and epididymus or in the cervix, urethra

and Bartholin glands. They are usually quiescent, but may become active after sexual intercourse, alcoholism and menstruation. The true carrier lesion is one in which there is a local lesion but a general immunity.

Diagnosis

Social circumstances and history may suggest the examination. Local examination may reveal a focus. The final diagnosis is either bacteriological or serological, but in either case difficulties may be met. The specimen should be obtained as directly from the lesion as possible. Definite Gram negative intracellular cocci in discharge from the genital organs is practically diagnostic. In some cases the organisms can be isolated by cultures and confirmed by cultural and serological reactions. Too often a few cocci may be found extracellularly which cannot be isolated in pure culture. The unsatisfactory nature of this situation was recognized by the Inter-Departmental Social Hygiene Board and work along these lines was encouraged. A precipitin test was devised which consisted in the testing of an autolyzed exudate against a known serum. It gives clear cut results at times, but is not entirely specific. The complement fixation test is also useful if positive, but is often negative in known carriers. Altogether the detection of the carrier is not very satisfactory, but something can be done. Regional location of foci is necessary after the organism has been found or serological evidence of its presence has been obtained.

Treatment

The usual local antiseptic treatment is indicated. New mercury compounds (Young) have more than ordinary promise. Specific treatment is uncertain but has followers. Non-specific treatment also has its advocates. Local treatment after identification of foci is most helpful.

Marriage should not be allowed until the possibility of the carrier state has been ruled out.

3. OTHER VENEREAL DISEASES

Carriers of Ducrey bacilli are not definitely known. If we admit a fourth venereal disease in the fusospirillary infection, the carrier relationships of this infection are unknown, but probably resemble those in Vincent's angina.

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PART III
SUMMARY

CHAPTER XVI

The Relations of Phorology to Preventive Medicine

1. the place of carrier work in preventive medicine

Preventive medicine, as applied to the infectious diseases, has a many sided program which is daily producing results. This program may be outlined as follows:

A. Prevention of the spread of parasites from the point of multiplication which is usually in the host. This procedure involves early treatment in the home or hospital, the disinfection of infectious discharges, isolation and quarantine.

B. Prevention of the spread of parasites in the environment. This is one of the aims of sanitation and includes the disinfection of food, drink, air and the destruction of insects.

C. The personal prevention of attacks by parasites, or personal hygiene. This field includes the increase of personal resistance and the avoidance of risks of infection.

D. Specific immunity by vaccination or serum prophylaxis.

Any one of these measures if logically and completely carried out would put an end to an infectious disease, but it would be day dreaming to imagine that any one or all of these measures can be completely carried out for all infections. However, by suitable selection of means for ends, many solid results are being obtained.

Carriers come under consideration in each part of this program.

A. The measures which have been so effective against case transmission are equally effective against carrier transmission. Some cure themselves under quarantine or observation, others can be cured by treatment. The relative amount of attention which should be paid to cases and carriers from this point of view has been considered under each disease. The program of course includes the diagnosis of carriers and this is one of the limitations of this method for carriers as it is for cases. To really diagnose and treat every case and carrier of an infectious disease, especially during an epidemic, would require an organization which would

break down of its own weight. There would have to be a laboratory at every corner and an inquisition in every home. A medical officer of a transport once estimated that if ideal ventilation was provided on all parts of the boat, all the power would be used up on fans and the boat would be standing still in the middle of the ocean. The same absurd conclusion would be reached by trying to enforce the carrier program to the bitter end. As was evident during the war, the work of detecting and handling carriers was often out of the question on account of the amount of work and the interference with the aim. Life must and will go on spite of infections. On the other hand, a more modest attempt is often feasible and effective on a small scale. While, therefore, this method is logically and practically effective within limits, it alone cannot be counted on to prevent disease.

B. Granting that other measures are necessary, sanitation accomplishes a great deal and must be directed against carriers as well as against cases. The relative amount of protection necessary against carriers cannot be accurately stated, because the dangers are unknown. A water supply must be unnecessarily chlorinated for many days of the year in order to be safe for the whole year. Sanitation undoubtedly cuts off many sources of infection from carriers in water, milk, food and air. The limitations of this method are its breakdown at critical lines due to accident or human weakness and to its failure to cover contact infection. We have at present no means of sterilizing respiratory droplets in the air of street cars or movies.

C. Personal hygiene has advantages and limitations as applied to carriers. It usually consists of two parts, the maintenance of resistance and personal care to avoid infection. The maintenance of a clean nose and mouth is of advantage as it is a partial protection from becoming a contact carrier. Care in personal habits is effective against carriers as against cases. There are limitations to this part of the program, however, as is shown in the recent development of "bacteriophobia." Some individuals, including even physicians, have become so particular about exposure that they have lost their value as social beings. The soldier cannot think of personal hygiene as applied to war injuries. There are, however, practical and reasonable applications which are of value.

For the carrier himself personal hygiene means preventing the exposure of others to his own infection.

The following is a summary of rules:

a. For fæcal and urinary carriers:

(1) Deposit feces and urine only in places provided for such a purpose and not where they can knowingly infect a water supply.

(2) Wash hands with soap and water after going to the toilet. Use individual paper or towel.

(3) Wash hands before each meal. Use individual eating utensils.

(4) Do not engage in food handling occupation.

(5) Disinfect soiled underclothing in 5 per cent carbolic acid solution.

(6) Do not use common bath tub; use sponge or shower bath.

(7) Report to physician for periodic examination.

b. For the respiratory carrier

(1) Dispose of discharges from nose and throat in a safe way, in spittoon or handkerchiefs. Do not spit promiscuously.

(2) Use personal eating utensils.

(3) Wash hands when soiled with respiratory discharge. Use individual towel.

(4) Avoid close contact in talking; avoid kissing.

(5) Report to physician for treatment and regular examinations.

c. For genito-urinary carriers

(1) Avoid sexual intercourse, unless with protection.

(2) Do not marry without permission of a physician.

(3) Take regular treatment.

(4) Have periodic examinations.

d. For the blood carrier

(1) Avoid bites of mosquitoes by screens and bed nets.

(2) Kill mosquitoes found in room.

(3) Follow lines of treatment.

(4) Have periodic examinations.

D. Vaccination. This is one of the best all around measures of preventive medicine as the chemistry of the body is made immune. This immunity is of course effective against carrier strains as well as case strains. Its limitations lie in the fact that there are many severe diseases against which no vaccination is available and the

fact that the immunity to smallpox and typhoid is relative and temporary. The immune person may also become a contact carrier, but this condition is usually temporary.

The combination of all these methods is very effective and prompts the enthusiast to draw pictures of a disease free world. The place of carrier work in this program should neither be exaggerated for its own sake nor minimized in favor of other measures. It should be given its proper value in the major project.

2. THE METHOD OF CARRIER WORK

1. The first and most obvious place to start carrier work is with the case. If a case can be diagnosed by demonstration of a parasite, a carrier can be detected by the same methods. The list of diseases in which release examinations can be made is small in comparison to the total number of diseases but large in comparison to actual practise. Some few diseases, such as diphtheria, are covered by law or regulations, but others, as typhoid, are left to the practitioner's judgment. A great advance will be made in carrier work when release cultures are insisted on whenever possible. Convalescence has several advantages for carrier work. There is usually plenty of time for careful examination. Early diagnosis is possible before any harm is done and treatment is easier, as it joins on to the treatment of the case.

A single adequate examination after an infectious disease would be sufficient to dispose of the carrier question. For example, a single adequate examination of bile ducts after typhoid, or of the nasopharynx after diphtheria or meningitis would in the great majority of cases be sufficient, but usually specimens and examinations are more or less inadequate. Several release examinations are therefore wisely insisted on. The specimens should be taken, if necessary, by a "phorologist" who is interested in finding the parasite, rather than by a physician who may be chiefly interested in receiving a negative laboratory report.

2. The next logical step is to examine contacts. This examination has a double object. On the one hand, it may be possible to pick up the carrier who has caused the case in question, or, on the other hand, it may be possible to diagnose other carriers who have been infected by the case. The extent to which this work

should be carried must be determined by the indications and common sense. The problem is fairly easy in a small group such as a family, but becomes more difficult in schools, offices and among troops. As laboratory facilities increase, this phase of the work tends to increase. As experience increases, we will be more able to give a more exact program.

3. In addition to the case and the contacts there are several general measures which are practical and valuable. The first of these is the examination of special groups such as food handlers. If the amount of sickness due to ignorant and careless servants were accurately known, it would probably be a shock to most people. The worst conditions are usually found in the colored races. Public eating places as well as homes are subject to contamination in this way. These examinations should relate primarily to intestinal carriers, but milkmen should be examined for diphtheria carriers and possibly streptococcus carriers.

4. Another practical line of carrier attack is in applicants for positions. They are usually subject to some examination and the common carrier conditions can gradually be included. As more exact methods are becoming available for the evaluation of the individual, it is being realized as never before that a real examination should include the whole organism, mental and physical. If we go one step farther and view the individual as a social being, it is also indicated to determine whether he is a carrier. The actual examinations to be made should depend on previous sickness, the nature of the work and the prevailing diseases. Under varying conditions these examinations should include the following procedures: (1) A nose and throat swab could be made and blood serum tubes could be inoculated for growth of the diphtheria bacillus. (2) A tonsil swab could be made and the specimen examined on a blood agar plate for hemolytic streptococci. (3) A nasopharyngeal swab could be made and the material examined on laked blood agar plates for meningococci. (4) The saliva could be examined for pneumococci by the mouse method. (5) The feces and urine could be examined for typhoid group of bacilli. (6) The feces could be examined for the organisms of cholera and dysentery. (7) A blood film could be examined for malarial gametes or filaria.

5. A similar time and place for carrier work is at the regular physical examinations which are becoming more and more frequent. These examinations are usually made for the personal benefit of the individual but should be broadened to include the welfare of the group. The success of the work would depend naturally on the common sense and care with which it was planned.

6. A special case is presented by carriers in the venereal diseases. Recently a demand for premarital examinations has arisen to meet this situation. In spite of its difficulties this movement is a real advance. It calls for examinations for syphilis, including the Wassermann reaction, and examination for the gonorrhea, including specimens of prostatic secretions. If these examinations were more general and if appropriate action followed the results, the number of social tragedies and divorces would be appreciably reduced.

3. CARRIER WORK IN THE MILITARY SERVICES

On the technical side, carrier work in the military services is of course the same as elsewhere, as the putting of a uniform on the host does not affect the parasite. There are, however, several special factors in epidemiology and administration among soldiers which do affect the work in a peculiar way. Personal contact is much closer and more constant among troops in barracks or in the field than among private citizens. Hence, the chances for the functioning of carriers are particularly good. On the other hand, diagnostic and control measures, when approved, can be carried out more exactly on account of military discipline. Again, the high standard of laboratory facilities which has been maintained in the United States Army since the days of Sternberg tends to make carrier work easier than in some other places. It may, therefore, be said that conditions in the Army, and the same is true of the Navy, offer unusual need and opportunity for carrier work. The drawbacks are lack of time for proper examination, lack of facilities for the mass of work and lack of control due either to an emergency or to official non-support.

Beginning with the case, release examinations can usually be made with certainty. Regulations insure the sending of specimens to the laboratory and the laboratory work is usually prompt

and reliable. In fact, three release cultures of feces and urine after typhoid infections have been made for years in the Army as a result of the early efforts of Russell. The Malarial Register, introduced by Craig, has also served to emphasize the carrier aspects of malaria. Release cultures are also of course made routinely in convalescents from diphtheria and should be the rule after meningitis, dysentery and cholera.

After an epidemic, the number of temporary convalescent carriers may be so large as to be a problem. It may be necessary to send men to duty as soon as possible, but carriers should be held if possible until clean. The alternative of discharge for disability should be taken only as a last resort. A public service owes it to the individual and to the country to do as much as possible for the carrier state. If discharge becomes necessary, the public health officials of the place to which the man goes should be notified.

Recruits offer a large opportunity for carrier work. It is being realized more than ever that the raw recruit is first of all a medical problem. He should be examined for mental and physical suitability; minor defects should be corrected. He should be immunized against smallpox and the typhoid fevers. Wassermann reactions have been done routinely in the past and Schick tests are now in order. Altogether about two weeks time could be taken up by the medical officers in preparing the recruit for the work in hand. The preparation of a recruit's tissues by the correction of defects and the training of his immune mechanism by the medical officer is as necessary as the training of his neuromuscular apparatus or his morale by the line officer. Carrier work is another measure of preparation for social enterprises. The detection of carriers should be done early in order to pick up chronic convalescent carriers before any harm is done. On account of the numbers, it may be necessary to confine the examination to those who give a previous history of diphtheria, meningitis, typhoid or dysentery or malaria, or who come from infected districts.

When cases occur, the examination of contacts is indicated, but its degree of application is a difficult question. A complete examination is of course the logical measure, but it is usually out of

the question and practical experience shows that other less radical measures are sufficient. Attempts to examine contacts should usually be confined to immediate contacts only, unless the group is small, or unless the laboratory facilities are unusual, or unless other measures fail, such as general sanitation and hygiene.

In any effective carrier work, some continuous record is necessary by which a chronic carrier can be checked up by different medical officers under whose observation he may come. In the Navy, the Health Record would serve admirably for this purpose. The Army has as yet no record of this kind, except the Syphilitic and Malarial Registers. Efforts to introduce a Health Record have so far been defeated by the amount of work necessary for keeping it properly. There is, however, the individual Service Record which has in the past had some data on vaccination. It has now been decided to give more space for medical records which will include a place for carrier examinations. In this way the carrier status of the individual can be checked up by each medical officer who reviews the records.

During the war, carrier work eventually reached a high state of technical perfection as so many well trained medical officers and assistants were available. The degree to which the carrier program was actually used to control the situation varied with the circumstances. Now that the military establishments are contracted to a peace basis, this work has necessarily become limited. But since the work of the military organizations is now largely educational in connection with National Guard and the Reserves, the principles learned should not be forgotten. This new knowledge should be applied on as large a scale as possible, as a measure of education and preparation.

PART IV

CARRIERS IN VETERINARY MEDICINE

CARRIERS IN VETERINARY MEDICINE

Carriers of the specific organisms of various infectious diseases met with in veterinary medicine have for a number of years been recognized among domestic animals. However, there is a marked paucity of literature treating of the subject generally. As a matter of fact, so far as I have been able to ascertain, there is not a single work published in English, French or German, dealing collectively with carriers of disease-producing organisms of veterinary subjects.

On the other hand, the carrier problem in a number of infectious maladies of domestic animals has been given careful consideration in studies of the individual diseases, and from our present knowledge of the subject, thus gained, it is clearly evident that carriers among veterinary subjects present a problem equal in importance to that in human medicine. Further, in numerous instances the animal carrier is a distinct menace to the health of human beings, so that often the problem is not only one of prevention of disease among lower animals, but of safeguarding the health of man as well.

For purpose of consideration in this section, carriers have been arranged in three principal groups. The first group includes carriers of organisms known to be pathogenic for man as well as for the lower animals. The second group deals with carriers of organisms which are pathogenic for lower animals and which may possibly prove pathogenic for man under certain circumstances. The third group includes carriers of organisms pathogenic for animals only. Under each main group are then taken up (1) carriers of bacteria, (2) carriers of protozoa and (3) carriers of filterable viruses.

CHAPTER XVII

Carriers of Organisms Pathogenic for Both Man and The Lower Animals

A. CARRIERS OF BACTERIA

1. Micrococcus melitensis

"Mediterranean," "Rock," "Undulant" or "Malta" fever in man, caused by Micrococcus melitensis, has for an indefinite period been more or less endemic on the Island of Malta. The disease has also been reported from Italy, Greece, Turkey, Spain, India, Africa and the Philippine Islands. In the United States it has occured in Texas along the Mexican border. The affection is primarily a disease of goats. Sheep, horses and cattle, however, are occasionally affected.

From the standpoint of carriers, Malta fever presents a highly important problem in those localities where the disease exists, as the infection is ordinarily transmitted to man through the ingestion of milk from animals harboring Micrococcus melitensis in their udders.

Zammit (1) demonstrated that approximately 10 per cent of the goats on the Island of Malta, though apparently healthy, were eliminating the micrococcus of Malta fever with their milk. Such milk, when fed to monkeys, even for one day, produced typical attacks of the disease, the manifestations of the affection in such animals closely resembling the symptoms noted in the disease in man.

Carriers also eliminate the organism irregularly in their urine. The disease may thus be readily transmitted to healthy animals through the ingestion of feed and water contaminated with the urine of carriers.

Mohler and Hart (2), in reporting the finding of carriers in an importation of 65 goats from the Island of Malta to the United States in 1905, state that out of 12 persons who were known to have

consumed milk from these goats during the voyage to this country, 8 developed Malta fever. The diagnosis was confirmed in 5 cases by the agglutination test, blood specimens not being obtained from the other 3 cases. The 4 individuals who failed to contract the disease drank only a small amount of the milk or partook of it only after it had been heated.

Upon arrival in the United States the goats in this shipment were placed in quarantine and specimens of their blood serum subjected to the agglutination test for Malta fever. Twenty positive and suspicious reactions were obtained. Subsequently positive results were obtained with specimens from a number of those animals whose blood had given negative results to the first test.

The milk of 8 typically positive reactors was examined bacteriologically and Micrococcus melitensis demonstrated in large numbers in 4 cases. The milk of these animals appeared absolutely normal and failed to show evidence of changes even on chemical examination. Examination of the urine revealed the organism in 1 out of 11 cases studied.

Habitat of the organism. Micrococus melitensis in the body of carriers lives a passive existence. In localities where the disease is prevalent a large percentage of goats, and in some instances sheep, harbor the organism in their udders, usually without changes in the gland tissue. In a number of cases the micrococcus is also found in the blood of apparently healthy animals and is eliminated in the urine. Rarely the organism is found in the intestinal tract.

Occasionally autopsy of carriers of the organism may demonstrate a slight fibrinous inflammation of the udder and in some few cases purulent foci. The spleen and certain of the lymph nodes, particularly the mesenteric and inguinal glands, may be found slightly swollen.

Detection and management. Carriers of Micrococcus melitensis may be detected through the application of the agglutination test and bacteriological examination of the milk, blood and urine of suspected animals. Saisawa (3) utilized the complement-fixation test for the detection of the infection. However, because of its relative simplicity, the agglutination test is more adaptable.

In carrying out the agglutination test either blood or milk serum may be used. Blood serum, however, is preferable. Mohler and Hart (2), after comparing the agglutinating titre of blood serum from normal and infected goats, considered complete agglutination within one and one-half hours in a dilution of at least 1:70, a positive reaction.

Several years ago Evans (4), in calling attention to the very close relationship of Bacterium abortus (Bang) to Micrococcus melitensis, pointed out that the serum of cattle infected with the Bang organism readily agglutinates the micrococcus of Malta fever. While at present there is no evidence that goats are commonly infected with Bact. abortus, the possibility of positive reactions in some instances being due to infection with the bacterium of Bang, should be borne in mind when carrying out the agglutination test for Malta fever.

For the bacteriological examinations a nutrose agar containing beef serum and of a slightly acid reaction, is best adapted for the isolation of the organism. The growth, however, is rather slow. Seventy-two hours or longer are required before the colonies are discernible to the naked eye.

Animals found to be carriers of Micrococcus melitensis are a menace to the health of both man and animals. In localities where the disease is not well established its spread should be guarded against by the prompt destruction of cases and carriers.

Where the disease is well established and a great number of the animals are infected, slaughter of carriers is not always feasible. In such cases the disease can only be controlled by the inauguration of measures to prevent direct or indirect contact of carriers with healthy animals.

As the disease in man is due, in essentially all instances, to the consumption of milk containing the organism, it is highly important that milk from known or suspected carriers of Micrococcus melitensis be properly pasteurized.

2. Bacillus tuberculosis

The disseminator of bovine tubercle bacilli is a serious menace to the health of man because of the susceptibility of young persons to infection with this type of the organism. In the vast percen-

tage of cases the infection is transmitted through milk. Transmission of tuberculosis from animal to man through the ingestion of infected meat, or meat-food products into the preparation of which may have entered glands or other tissues containing the organism, is very rare. In the first place the large percentage of meat consumed is cooked. Further, meat does not form a part of the ordinary diet of young children. Where eaten uncooked by adults, chance of infection is slight, because of the resistance of older persons to the infection with the bovine type of tubercle bacilli. Where vaccination of animals with human tubercle bacilli, as later described, is attempted, we have a different situation. In such instances the organism eliminated by vaccinated animals is capable of producing tuberculosis in both children and adults.

In tuberculosis we frequently meet with cattle which clinically manifest themselves as carriers but which are in reality occult cases of the disease. Such cases are often noted among dairy cows. Animals apparently in the pink of condition have been known to eliminate tubercle bacilli with their milk intermittently for years, the only indication of disease being a positive response to the tuberculin test. In other cases of this character tubercle bacilli are eliminated periodically for years with the feces, as a result of an occult pulmonary affection. In such instances the animal swallows material from the lungs containing the organism and passes it through the digestive tract. Autopsy of these cases demonstrates open lesions of a progressive nature. Animals coming into this category, when permitted to live for a considerable time, as a rule, subsequently manifest evidence of the disease and on autopsy well-marked lesions of tuberculosis, frequently generalized, are found. These cases cannot, therefore, be considered true carriers.

There is another condition met with in cattle in which certain animals may more properly be considered true carriers of the tubercle bacillus. Not infrequently, autopsy of cattle which have reacted to the tuberculin test, fails to demonstrate appreciable lesions of tuberculosis. Bacteriological examination and guinea pig inoculations, however, frequently demonstrate that certain of the lymph glands of such animals, while appearing normal, or at the most showing only minor changes, harbor the bacil-

lus of tuberculosis. Of 1296 specimens, practically all of which were such lymph glands, examined by the United States Bureau of Animal Industry (5) during the fiscal year 1921, a total of 258 or nearly 20 per cent were found to harbor tubercle bacilli. Such carriers are not a menace as disseminators of the infection, but are of importance from the standpoint that they may later pass from what might be termed an "incubationary carrier" state, develop the disease in a pronounced form, and then become spreaders.

Carriers of tubercle bacilli may be produced in dairy cows as a result of attempts at artificial immunization against tuberculosis. Some years ago considerable attention was paid by investigators of animal diseases to the so-called "bovo-vaccination" of cattle against tuberculosis. The treatment consisted of the intravenous administration of human tubercle bacilli which were not fully virulent, cattle possessing considerable resistance to the human type of organism. While such procedure materially raises the immunity of the animal to bovine tuberculosis, a large percentage of such cattle were found to harbor and eliminate the organism from their udders for years, without developing manifest lesions of the disease themselves, or at the most developing very minor lesions after tolerating the organism for a long period of time. Because of these dangerous carriers, produced as a result of this method of vaccination, the procedure did not become established in the United States.

The tubercle bacillus is frequently found in various of the lymph glands of hogs, occurring without additional lesions in other organs. In some such cases little or no abnormality is noted in the gland structure. In other cases, however, marked changes are found. Thus, as scrofula is a rather characteristic form of the disease in hogs, it is difficult to distinguish between what might properly be termed a carrier and an early case of tuberculosis of the glands. The bacillus of tuberculosis has also been occasionally found in the tonsillar crypts in hogs. Their presence in such location, however, is usually transitory.

Habitat of the organism. In those carriers among cattle which harbor the tubercle bacillus in glands, the submaxillary, cervical, prescapular, mediastinal, bronchial and mesenteric nodes are the

most frequent locations. Such glands may be more or less swollen and show small inflamed areas in the cortical substance.

In carriers produced as a result of vaccination against tuberculosis no detectable lesions may be found on autopsy, although the animal may have been eliminating the organism frequently with her milk. However, after a considerable period of time (3 or 4 years in some instances) small atypical tubercles may be found in the udder.

In hogs the submaxillary and superior cervical glands are favorite habitats of the organism. The bronchial, gastro-hepatic and mesenteric glands are less frequent locations. Where these glands show lesions, a type of hyaline degeneration is frequently seen, cross sections of such glands having a dendritic or arbor-vitae appearance. In other instances small areas of inflammation or small yellow foci may be demonstrated in the glands.

Detection and management. The subcutaneous, intradermic or ophthalmic tuberculin tests, or combinations of the same, constitute the only means at our disposal for the detection of the carrier type of animal harboring Bacillus tuberculosis in its glands. Obviously, however, such tests will not differentiate these carriers from the more marked cases of tuberculosis. Further, while a considerable percentage of animals carrying the organism in their lymph glands will respond to the tuberculin test, negative results are undoubtedly obtained in a percentage of such cases.

Where vaccination against tuberculosis has been practiced, bacteriological examinations and guinea pig inoculation tests with milk specimens from suspected carriers, prove satisfactory for their detection. These tests must be frequently repeated, however, where negative results are obtained, before concluding that the animal is not eliminating the organism. Some of these carriers will also give a positive response to the tuberculin test.

The prompt slaughter of cattle and hogs known to harbor the tubercle bacillus is the practice to be recommended. Except in cases of valuable breeding stock, such hogs would ordinarily be butchered as an economic procedure. With cattle, however, this method cannot always be carried out because of the common practice of a large number of dairymen to maintain herds containing tuberculous cows. Under such conditions rigid measures

should be taken to prevent the exposure of healthy animals to these carriers of tubercle bacilli.

Because of the pathogenicity of the bovine type of tubercle bacillus for children, and the part that milk can play in the transmission of the infection, pasteurization of milk from herds in which there are animals known or suspected of harboring the bacillus of tuberculosis is obviously of utmost importance.

3. Organisms of the Salmonella, Enteritidis or Gaertner group

Bacillus enteritidis (Gaertner), Bacillus paratyphosus "B," Bacillus suipestifer, Bacillus aertrycke, and other members of the Salmonella group, have at different times been found associated with a variety of pathological conditions in cattle, horses, sheep, hogs and other animals. Further, carriers of these organisms have been frequently found among animals which have recovered from such affections, as well as in animals with no history of disease. Because of the rôle organisms of this group play in the production of "food-poisoning" in man, carriers of the same are of particular importance.

B. enteritidis has been occasionally found associated with severe cases of dysentery, especially in calves, although adult cattle are sometimes affected. Mohler and Buckley (6) in 1902 found B. enteritidis to be the etiological factor in an outbreak of enteritis with marked symptoms of intoxication, in a stable of twenty-one cows. This organism has also been found in pathological conditions of the udder, persisting in some cases for considerable periods of time after the disease process has subsided.

In hogs, Bacillus suipestifer is found as a complicating factor in cholera, the primary cause of the disease being a filterable virus. Carriers of this bacillus are very frequently found.

Among experimental animals the writer has noted an outbreak of disease among guinea pigs due to Bacillus aertrycke, in which carriers of the organism were subsequently found. O'Brien (7) records an epizootic among stock guinea pigs at the Lister Institute due to an organism which he identified as B. suipestifer. Subsequent to the outbreak he demonstrated 5 of the recovered animals to be carriers, eliminating the organism intermittently for five months.

Members of this group of organisms are occasionally responsible for outbreaks of disease among rodents. Further, healthy rats and mice are often found to be carriers of the bacilli of this group, eliminating the same with their feces. Because of the opportunity afforded for the contamination of foodstuffs with fecal matter from rats and mice around abattoirs, refrigerator plants, butcher shops, etc., these carriers are of no little importance.

Heuser (8) examined 100 mice and found 5 or 5 per cent harboring B. enteritidis and B. paratyphosus "B." Zwick and Weichel (9) in examining 177 mice demonstrated 28 or nearly 16 per cent to be carriers of organisms of the Salmonella group.

Meissner, Berge and Kohlstock (10) report an interesting outbreak of dysentery among calves due to B. enteritidis. One of the recovered animals was placed in a pasture with a number of cows and shortly thereafter the disease broke out among the adult animals. The recovered calf was then examined and was found to be harboring B. enteritidis in its intestinal tract.

Outbreaks of food-poisoning in man in a number of instances have been definitely traced to animals disseminating organisms of this group. Savage (11) described an outbreak of food-poisoning occurring at Newcastle-under-Lyme in 1914, in which 468 cases with 2 deaths occurred. The malady was found to be due to B. enteritidis in milk consumed by the affected individuals. Investigation proved the source of the infection to be a cow which had recently calved, and which had an udder affection and abscesses in one of its legs. The serum of this animal readily agglutinated B. enteritidis. Subsequent examination demonstrated B. enteritidis in the urine and uterine discharge. After the outbreak a number of specimens of milk from this cow were examined and on two occasions B. enteritidis was isolated.

Aside from those cases in which organisms of the enteritidis group may be eliminated with the milk, contamination with fecal matter often occurs at the time of milking through the dropping of particles of manure from the hair of cows which have not been properly cleaned, or through splashing at the time of defecation.

As regards meat, ample opportunity is often afforded for fecal contamination of such food in the slaughter-house during the course of its preparation. Thus carriers harboring members of

this group of organisms in their intestinal tracts may infect their own tissues or those of other animals at the time of slaughter, thereby indirectly menacing the health of man.

Habitat of the organism. In the larger percentage of cases, carriers of organisms of the Salmonella group harbor the same in their intestines, usually without appreciable tissue changes in the carrier state. Occasionally, small necrotic foci containing organisms of this group have been demonstrated in the spleen and liver of cattle, sheep and hogs.

In hogs which have had the intestinal form of cholera, ulcers of variable size (lental to as large as a quarter) which are slow to heal, and which usually harbor B. suipestifer, are often found, especially in the cæcum and large intestine. These ulcers usually occur as round, slightly projecting masses, of a yellow, brown, or almost black color, the cut surface appearing laminated from the periphery towards the center. Microscopically, sections cut perpendicularly through the ulcer show the thickened submucous tissue to contain numerous dilated capillaries and a large number of round cells. Above this is a thin layer of deep staining amorphous material. The uppermost layer is made up of necrotic material containing large numbers of bacteria of different type. B. suipestifer may be found in the necrotic material and frequently in large numbers around the periphery of the ulcer between the necrotic and healthy tissue.

Organisms of this group are occasionally found in the udder, usually following some type of udder trouble for which it was responsible, and rarely when there is no history of disease. Where such carriers have had a pathological process in the udder, tissue changes, characteristic of previous glandular inflammation, frequently exist.

In the B. aertrycke infection noted by the writer the organism was found harbored in the gall bladder. The walls of the bladder in most instances showed a marked catarrhal thickening.

Detection and management. Carriers of bacilli of the Salmonella group, harboring the same in their intestinal tracts and udders, as a rule, may be detected through the employment of ordinary bacteriological methods. Repeated examinations, however, must be made in some instances before the organism can be

demonstrated. The agglutination test may prove of some help in identifying animals suspected of carrying certain members of the group. Further, the writer was able to obtain complement-fixation reactions with blood serum from guinea pigs harboring B. aertrycke in their gall bladders.

Animals known to be carriers of organisms of the Salmonella group which are capable of producing disease in other animals, should be kept isolated until they are proven no longer a menace. In cases in which the organism is carried in the udder, irrigation with mild antiseptics may prove of value in eliminating the foci of infection. Occasionally bacterins or vaccines give good results. Administration of intestinal antiseptics has been resorted to in an effort to eliminate offending organisms harbored in the intestines. Such treatment, however, is not particularly promising of results. The slaughter of persistent carriers which continually cause trouble, is sometimes the most economic procedure.

Particular consideration should be given to measures for the prevention of infection of man. Milk from cows harboring organisms of this group is a particularly dangerous food for both man and animals. It should be remembered that Bacillus enteritidis (Gaertner) produces a toxin which is unaffected by pasteurization.

Because of the possibility of milk becoming contaminated with particles of fecal matter, during the milking process, cows know to carry organisms of the Gaertner group in their intestinal tracts are dangerous animals to supply milk for human use and should be eliminated as a source of milk supply while thus harboring and eliminating these organisms.

In the slaughtering of food-producing animals every precaution should be taken to prevent the contamination of carcasses with fecal matter. Particular attention should be given to measures to prevent meat and other food products from becoming contaminated with the excrement of rats and mice.

4. Bacillus tetani

The horse is a well-known carrier of Bacillus tetani. Cattle, sheep and hogs, however, also harbor the organism in their intestinal tracts and eliminate the same in considerable numbers in

their feces. Further, it has been demonstrated that the tetanus bacillus is not infrequently carried by smaller experimental animals (rabbits and guinea pigs). The organism has a very extensive distribution in nature, being a common inhabitant of the soil, especially where the same contains manure, particularly that from horses.

It is the opinion of some investigators that soil contains the organism only after receiving deposits of manure from horses or other herbivora harboring B. tetani, or where it is indirectly contaminated with drainage from areas containing manure of such carriers. This, however, is not likely. Because of the large percentage of carriers among herbivora, the tetanus bacillus is found more abundantly in earth containing manure, but it is nevertheless found in soil undoubtedly free from such fecal contamination.

The percentage of carriers among animals in different locations varies between rather wide limits. Park and Williams (12) state that approximately 15 per cent of horses and calves in the vicinity of New York City harbor the tetanus organism in their intestines.

On various stock farms it is often notable that tetanus almost invariably follows minor wounds not properly treated. In other localities such occurrence of the disease may be extremely rare.

Habitat of the organism. In carriers Bacillus tetani is found in the intestinal tract, especially in the large intestine. As is the case with a number of organisms harbored in the intestines, the tetanus bacillus under normal conditions, causes no disturbance in the health of its host and produces no change in the intestinal tissue.

While the horse commonly harbors B. tetani it is, nevertheless, very susceptible to tetanus. This type of carrier, in a way, is a mechanical carrier, as differentiated from the immune and convalescent types.

Detection and management. No particular difficulty is experienced in demonstrating the tetanus bacillus in the excreta of carriers by bacteriological examination and through the inoculation of mice, guinea pigs or rabbits.

It is obvious, of course, that with tetanus we are confronted with an organism which exists practically everywhere and of which

thousands of carriers exist and are coming into being daily. It is, therefore, highly important that particular attention be paid to wounds which have directly or indirectly come in contact with manure and soil or admixtures of the same.

5. *Bacillus oedematis maligni* ("*Vibrion septique*")

The anaerobic Bacillus oedematis maligni, or "Vibrion septique" as it was called by Pasteur, is widely distributed in nature and is frequently found in the intestinal tracts of normal cattle, horses, sheep and hogs.

Among animals, malignant edema, the specific disease of this organism, frequently results from the infection of contused, lacerated, incised and other types of deep wounds, with soil, feces of carriers, or other material containing the bacillus of malignant edema. The disease sometimes follows castration and shearing. Further, it is an occasional complication of difficult parturition, where help is given the animal and proper precautions are not taken to prevent the introduction of infection with the hands and instruments. The disease also occurs in man following the contamination of wounds with soil, manure, or admixtures of the same.

Habitat of the organism. Carriers of Bacillus oedematis maligni, as stated above, harbor the organism in their intestinal tracts. Under normal conditions the bacillus lives a purely saprophytic existence in the intestines of such carriers, producing no tissue changes whatever as a result of its presence there.

Detection and management. The bacillus of malignant edema can usually be demonstrated in the feces of carriers through anaerobic cultural methods and animal inoculation tests without difficulty.

As this organism is found constantly in soil and is carried by a large number of animals of different species, sanitary measures must be relied upon to control the infection, as the elimination of carriers is obviously impossible. Particular attention should be paid to severe wounds contaminated with manure or soil.

6. Bacillus anthracis

While at the present time nothing is known of possible carriers of the anthrax organism among cattle, horses and sheep, it has been definitely established that apparently healthy hogs occasionally harbor Bacillus anthracis in various of their lymph glands.

Fortunately, the organism thus localized is not capable of being eliminated continuously to the outside world. However, such carriers are, nevertheless, of considerable importance; first, because they may later develop the disease in an acute form, thus disseminating the infection, and secondly, because such glands entering into the preparation of "cured" meat-food products, may produce the disease in man consuming such food, especially when uncooked.

Habitat of the organism. In hogs harboring Bacillus anthracis the organism is found most frequently in the mesenteric group, often only a single gland in the group being affected. Less frequently the cervical glands may be the seat of the infection. Occasionally the bacillus may be demonstrated in the submaxillary glands.

Glands containing the anthrax organism, as a rule, are more or less enlarged, and on cross section they appear of a brick-red color or they may be permeated with small, grayish-yellow, necrotic foci. The surrounding connective tissue may disclose a sero-edematous infiltration.

Detection and management. In the absence of allergic or other specific tests for anthrax, it is impossible to detect, during life, hogs which may be carrying the anthrax organism in their lymph glands. Consequently we are without means to prevent the possible introduction of such carriers in the midst of healthy hogs.

When carriers of this character are butchered in establishments where meat inspection service is maintained, the veterinary inspector has the opportunity to detect some of those cases which show appreciable lesions of the glands. However, in some instances the tissue lesions are so insignificant they may escape detection. It is obvious, therefore, that in order to prevent the possible infection of man, the added safe-guard afforded by thoroughly cooking various "cured" products before consumption, is advisable.

7. *Bacillus mallei*

While no definite, clear-cut carrier problem has been recognized in glanders, this disease is one of those maladies in which it is occasionally difficult to determine whether or not a particular infection can properly be placed in the category of carriers.

Autopsy of animals which have reacted to the allergic or serological tests for glanders, frequently reveal in the lungs, and occasionally in the liver or spleen, glanders nodules in an inactive or apparently arrested stage. Sometimes only a single nodule of such character is found. Very frequently it is impossible to isolate B. mallei from some of these lesions. On the other hand, in some of these arrested cases it is possible to demonstrate the organism bacteriologically and through guinea pig inoculation. In such case we are possibly justified in concluding that the animal in which this type of lesion was found was a carrier. Should it have been permitted to live and mingle with other animals it may have subsequently initiated an outbreak of glanders through development of the disease in an active, communicable form from this focus.

Habitat of the organism. In such instances, as described above, the lesions are most commonly found in the lungs. However, they are occasionally found in the liver or spleen. They occur as small, gray, shining nodules, rarely larger than a pea, the center often appearing pale yellow as a result of necrosis. The nodule is walled off from the normal structure by fibrous tissue.

It is often very difficult to differentiate the nodule of glanders from those caused by parasites. Microscopically, however, eosinophilia is a characteristic finding in parasitic nodules. Further, in parasitic nodules of recent origin fragments of the parasite may often be demonstrated, while in older processes there is usually calcification. Calcification in glanders nodules is doubtful, a number of investigators maintaining that it never occurs. It is certainly not a common finding. Demonstration of B. mallei in the nodule, of course, definitely establishes its nature. Failure to demonstrate the organism, however, would not in itself prove that the lesion was not that of glanders but obviously eliminates it from consideration as a carrier lesion.

Detection and management. The allergic and serological tests must be depended upon for the detection of carriers of Bacillus mallei as here considered. Fortunately, these tests give excellent results in the great percentage of cases. They do not, of course, differentiate between the active and arrested case. However, as the destruction of both active and inactive cases is advisable, this shortcoming of the diagnostic methods at our disposal, is of little consequence.

Suspected animals should be tested with intradermic or ophthalmic mallein, and in the case of suspicious or doubtful reactors, serum specimens from the questionable animals should be subjected to the complement-fixation and agglutination tests for glanders. A positive reaction to any one of these tests warrants the destruction of the animal.

8. Bacillus diphtheriae

While it has been proven beyond all doubt that true diphtheria in man and the common diphtheritic affections of lower animals, are distinct and separate entities, diphtheria due to infection with the Klebs-Loeffler bacillus occasionally occurs in animals coming in contact with individuals of the human family suffering from the disease. Considerable reference is made in the literature to cases of diphtheria occurring in cats, dogs, fowls, etc., as a result of infection with the organism of human diphtheria. Further, occasional transmission of the disease from animal to man has undoubtedly occurred.

From the standpoint of carriers, the house cat has been frequently incriminated. No information, however, is available as to the possible length of time the organism may persist in the body of such carrier.

Savage (13) has pointed out that diphtheria-like organisms may often have been taken for the real diphtheria bacillus in reports of cases and carriers of the infection among cats where the bacteriology of the case was not thoroughly worked out. He even goes so far as to conclude that it has not been satisfactorily established that cats develop diphtheria due to the Klebs-Loeffler bacillus or are carriers of the infection. There is, however, ample evidence of a definite nature to refute such conclusions.

Simmons (14) reports a fatal case of diphtheria in a woman, apparently contracted from a cat which was permitted to sleep in her bed. The cat had been sick about a week before the woman became ill. It had a croupy cough, was unable to swallow food and continually cried. The condition persisted for approximately two weeks after which the animal appeared to improve. Cultures from the throat of both the woman and cat demonstrated the presence of Klebs-Loeffler bacillus, the identity of the organism in both instances being definitely established through immunologic tests carried out with guinea pigs protected with diphtheria antitoxin. The cat was chloroformed and autopsied and B. diphtheria recovered from a lesion in the nasal fossa.

A second cat which had been associated with the animal just referred to, was found to harbor true diphtheria bacilli in lesions of the vocal cords.

Habitat of the organism. Cats which are found to be carriers of the Klebs-Loeffler bacillus, harbor the organism in their nose or throat. In one of the two cases described by Simmons, a small oval ulceration, covered with a yellowish-gray pseudomembrane, occurring between two smaller red inflammatory areas, was noted in the left nasal fossa. In the second case described by this author, small, elongated, grayish-white patches of pseudomembranes were found covering ulcerations of the vocal cords. These patches were surrounded by a red inflammatory zone.

Detection and management. In examining cats suspected of harboring the diphtheria bacillus, material should be obtained from the throat and each side of the nose with sterile swabs and 3 or 4 tubes of Loeffler's serum media inoculated with each swab. These cultures should then be incubated and subjected to the usual bacteriological examination for Bacillus diphtheriae, care being taken not to mistake pseudo-diphtheria organisms, frequently found, for the Klebs-Loeffler bacillus.

Cats demonstrated to be carriers of the organism of human diphtheria are obviously a menace to the health of human beings, especially the child who plays with the animal. Although there are no records of the isolation and treatment of such carriers, it is probable that a number of these cases would clear up under proper treatment. However, under ordinary circumstances, prompt destruction of recognized carriers is the policy to follow.

9. Bacillus pestis

While bubonic plague ordinarily occurs as an acute affection in rats, in localities where the disease is endemic apparently healthy rats may occasionally be found harboring Bacillus pestis in foci in their abdominal viscera.

The Indian Plague Commission (15), in examining a large number of rats caught in two villages where plague had recurred annually without discoverable reinfection, found 6 apparently healthy animals with small abscesses in their abdominal cavities, containing virulent plague organisms. These rats were all trapped within two months, at a time of the year when, so far as could be ascertained, plague did not exist in man nor rats in the two villages in question.

McCoy (16) found 13.8 per cent of several hundred ground squirrels examined for plague lesions, harboring B. pestis in purulent foci in one or more lymph glands, with no additional evidence of disease. In squirrels experimentally infected, similar lesions (referred to by McCoy as "residual buboes") were observed in the majority of animals which survived the infection.

Rats and squirrels with such lesions have ordinarily been looked upon as chronic cases. Nevertheless, without drawing the line too close, the animal with small, entirely localized lesions of an inactive character, which give rise to no manifest disturbance of health, may properly be considered a type of carrier.

From present knowledge, it is difficult to say just how much importance should be attached to such carriers of Bacillus pestis. Apparently they are not a serious menace. Whether or not the organisms persisting in these abscesses are ever capable, under certain conditions, of subsequently inciting an acute attack of plague, thus permitting of its spread, is a matter of conjecture. However, the carcasses of rats with such lesions, dead from some other cause, may be eaten by susceptible rats and thus give rise to an outbreak of the disease.

Habitat of the organism. The lesions of Bacillus pestis in rats harboring the organism, are usually found in the spleen, liver, mesentery and pelvic glands. They occur as small abscesses containing a creamy or cheesy pus. Often adhesions are found between the affected area of the spleen and the mesentery.

In squirrels, McCoy found the median, posterior inguinal and pelvic glands the most frequent seat of the infection. Less frequently lesions were found in the cervical and axillary glands. The gland may appear as a mass of slightly yellowish pus as large as a pea. In other instances the purulent mass is much smaller, or there may be noted only a few, mustard-seed size, necrotic points.

Detection and management. Rats and squirrels harboring the plague organism in these chronic lesions have not been noted to manifest appreciable disturbances of health. Obviously, the detection of such carriers in localities where plague occurs or is suspected, is accomplished by the examination of considerable numbers of trapped or shot rats and squirrels. Bacillus pestis, ordinarily, can readily be demonstrated in the lesion bacteriologically and through animal inoculation tests.

Rodents carrying B. pestis in lesions such as above described, apparently are not a serious menace, and no special means have been employed for the control of such cases. However, in districts where plague has existed, the possibility of recurrence through such animals must be considered, and so far as rats are concerned, should serve as a stimulus for continued sanitation and measures contributing to the extermination of rats, even though an organized extermination campaign is not in progress.

10. Bacterium tularense

McCoy (16) in examining ground squirrels for evidence of plague, found lesions which could have readily been mistaken for those of that disease. Subsequently the causative organism was isolated by McCoy and Chapin (17) and named Bacterium tularense, they adopting such name because it was in squirrels from Tulare County, Calif., that the disease was first noted.

Man is readily susceptible to infection with this organism either by insect bites or direct inoculation into abrasions. A local lesion is produced with glandular swellings and continued fever. The mortality is low.

While lesions of the disease may be found in the spleen, liver, lungs and lymph glands, a number of squirrels were found harboring the organism in a single bubo. Such animals are carriers in

the same sense as rodents harboring B. pestis in residual buboes. The infection has also been found in jack rabbits.

Habitat of the organism. In those animals which may be classed as carriers, Bact. tularense is harbored in one or more buboes, the inguinal, pelvic, axillary and cervical glands being most frequently affected. McCoy states that these buboes in the squirrel are usually as large as a pea, sometimes larger. They are rather firm and when cut present a dry, yellowish, or blood-stained surface. Some hemorrhage is frequently found in the surrounding tissue. The gland structure is, as a rule, replaced by a firm, caseous mass. Purulent glands are uncommon.

Detection and management. The organism can be definitely identified in affected glands through bacteriological means and animal inoculation tests. Bact. tularense is a very difficult organism to cultivate, the common types of media being unsuitable for its growth. McCoy and Chapin found, however, that it could be cultivated on an egg medium made entirely of the yolk. The organism appears as a minute rod 0.3 to 0.7 micron in length and is frequently capsulated. It stains best with carbol-fuchsin or gentian violet.

Little is known as to the importance of Tularemia in squirrels or rabbits and no special measures have been employed for its control.

11. Bacillus erysipelatis suis

Swine erysipelas, caused by Bacillus erysipelatis suis, is an important disease of swine in European countries. Recently, however, the disease, in a mild form, has been definitely recognized in the United States. It usually manifests itself as an acute septicemia with a characteristic reddening of areas of the skin. A mild, urticarial form ("diamond-skin disease") and a chronic type are also recognized.

The carrier problem in swine erysipelas has been given considerable attention by European investigators and the fact definitely established that a large percentage of hogs in localities where the disease is prevalent, are carriers of the organism.

Swine erysipelas occasionally occurs in man following infection of skin injuries. In such cases there is an erysipelas-like

reddening of the skin accompanied by a swollen condition of the neighboring lymph glands. At times, the skin lesions assume a blackish-red color and exfoliation of the epidermis occurs with exudation of serum. Swelling of joints in the region of such lesions may also be noted. Infection through ingestion of the organism either does not occur, or is extremely rare. Lubowsky (18) reports a case of jaundice and intestinal catarrh in a boy in whose feces he found large numbers of bacteria identical with B. erysipelatis suis. This may possibly have been a case due to infection through the alimentary tract although there was no definite proof of same. In man the disease usually terminates in recovery after 3 or 4 weeks. It may, however, persist for two or three months.

Habitat of the organism. The bacillus of swine erysipelas is frequently found in large numbers in the crypts of the tonsils of carriers. No lesions other than an occasional slight inflammatory process have been noted in such carriers.

In the intestines the organism is very frequently found in mucous plugs of the ileo-cecal valve. Olt (19), who has contributed considerably to our knowledge of carriers in swine erysipelas, frequently noted the bacillus in minor intestinal lesions caused originally by parasites, especially Strongyli.

Out of 50 apparently normal animals examined, Pitt (20) found 28 or 56 per cent harboring the erysipelas organism in their tonsils. In an examination of the intestines of 66 animals he found Bacillus erysipelatis suis in 26 or over 43 per cent of those examined.

Detection and management. Because of the large percentage of carriers in districts where the disease exists and the difficulty which is experienced in obtaining satisfactory specimens of tonsil secretions for bacteriological examination, routine examinations for the detection of carriers is ordinarily impracticable in such localities. In special cases, however, where valuable breeding animals are being introduced into territory free of swine erysipelas, bacteriological examinations should be made of "swabbings" from the throats of such animals during their quarantine period.

Examination of the feces can be carried out without difficulty, and in some cases will yield positive results where the bacillus is carried in the intestinal tract. However, as the organism is

eliminated only sporadically from the intestines, a single negative bacteriological finding, obviously, would not indicate that the animal was not a carrier.

The problem in those localities where the disease exists resolves itself into one of immunizing susceptible animals. Fortunately, good results can be obtained through vaccination against the disease. The method of Pasteur, giving two injections, twelve days apart, of a culture which has been attenuated by passage through rabbits, may be used, or the method of Lorenz and Leclainche, in which immune serum and virulent culture are administered simultaneously and followed in 12 days by an injection of culture alone, may be employed.

Cases of the disease in man have been confined to persons working around hogs in localities where swine erysipelas exists, and then only after minor skin injuries. Possible transmission of the disease to man from carriers can, therefore, be largely controlled through proper attention to tissue injuries.

12. Miscellaneous facultative-pathogenic bacteria

In addition to the various organisms of specific diseases already enumerated, animals are known to harbor in their upper air passages, intestines, genital tracts, and in the case of milch animals, in their udders, a considerable variety of pyogenic and facultative-pathogenic organisms. Under suitable conditions, in the body of their host, or in other animals or man directly or indirectly infected by such carriers, these bacteria are often capable of setting up various pathological processes. Included in this category are various types of streptococci, staphylococci, virulent strains of Bacillus coli, Bacillus pyocyaneus, Bacillus pyogenes, Bacillus botulinus, Bacillus aerogenes capsulatus, etc.

Habitat of the organism. Streptococci, Staphylococcus albus, aureus and citreus, and Bacillus pyocyaneus are among those organisms frequently found in the upper air passages of horses, cattle, sheep, swine, dogs, cats, etc.

Bacillus pyogenes, an organism which, under favorable conditions, is occasionally responsible for suppurative processes in the lungs, pleurae, peritoneum, etc., of hogs, arthritis in hogs and cattle, and inflammatory processes of the udder of cows, goats

and sheep, is frequently found in large numbers in the grayish, mushy plugs in the crypts of tonsils of healthy hogs.

Of the large variety of bacteria found in the intestines of horses, cattle, sheep, swine, etc., which have not been previously mentioned, and which may prove pathogenic under particular conditions, are virulent types of Bacillus coli, Bacillus lactis aerogenes, Bacillus proteus mirabilis, Bacillus pyocyaneus, Bacillus botulinus and Bacillus aerogenes capsulatus.

Virulent strains of Bacillus coli communis, Bacillus lactis aerogenes, Bacillus proteus mirabilis and Bacillus pyocyaneus, are frequently found as factors in cases of so-called "white scours" of sucklings, especially calves.

Bacillus botulinus is occasionally found in the intestinal tract of normal hogs. Such carriers are of importance because of the possible contamination of foodstuffs with particles of fecal matter from hogs.

Bacillus aerogenes capsulatus is frequently found in the intestinal tracts of healthy herbivora. This organism has not been incriminated as a cause of natural infection in animals, but is of importance as a factor in the infection of extensive wounds in man, especially war wounds.

Besides those organisms heretofore referred to as being harbored in the udders of cows and goats, Bacillus pyogenes, Bacillus phegmasis uberis, and various types of staphylococci, have been found in the udders of apparently healthy animals. These organisms are capable, under favorable conditions of producing inflammatory and purulent processes in the udders of animals, and under certain circumstances, may possibly prove pathogenic for man.

Detection and management. The organisms referred to in the foregoing paragraphs can practically all be readily detected in carriers through the employment of bacteriological methods usually utilized for the identification of the different members of this group, without difficulty.

Because they are chiefly facultative-pathogenic organisms and with one or two exceptions, are widely distributed, but little attention has been given to carriers of these bacteria.

B. CARRIERS OF PROTOZOA

1. Leishmania canis

In several localities where infantile Leishmaniasis, a tropical, febrile splenomengaly, or kala-azar of young children is prevalent, Leishmania canis, an organism indistinguishable from Leishmania infantum, has been frequently found in dogs. There are also rare instances of its occurrence in cats. Sergent, Lombard and Quilichina (21) found Leishmania in the bone marrow of a cat. The organism has been demonstrated in dogs in Tunis, Algeria, Italy, Sicily, Spain, Greece, Malta and Transcaucasia. The disease in canines is usually of a very benign character although some animals may show marked disturbances of health as a result of the infection. Frequently, however, Leishmania canis is harbored in the bodies of dogs showing no appreciable evidence of disease whatever.

There is considerable evidence tending to show that the parasite of Leishmaniasis can be transmitted from animal to animal by fleas. The probability therefore exists that carriers of the organism among dogs may prove a source of infection for man.

Habitat of the organism. The Leishmania harbored by dogs may be found in the endothelial cells of the spleen and liver, in the myelocytes and rarely in the leucocytes of the peripheral blood. In such cells they appear as numerous oval bodies 2 to 4 microns in length and 1.5 to 2 microns broad. Each organism contains a large nucleus and a smaller blepharoplast. Stained by Giemsa's method the large nucleus appears as a pale red body whereas the smaller blepharoplast stains a dark violet.

Detection and management. Very rarely an occasional polymorphonuclear or mononuclear leucocyte of the peripheral blood may be found to contain the parasite. Thus, in some few instances, careful examination of a number of blood preparations may prove successful in demonstrating the organism in carriers. Negative findings, however, are without significance.

Microscopic examination of material obtained by puncture of the spleen or liver is the only method giving promise of success in the majority of cases of actual carriers of Leishmania. In making the puncture, a fine, scrupulously clean, hypodermic needle attached

to a syringe by means of a small piece of rubber tubing, is employed. It is important that the needle be absolutely dry as a trace of water will distort or burst the parasite, making its recognition exceedingly difficult or impossible.

In the dog the dorsal end of the spleen does not vary in position. The position of the rest of the organ, however, is very variable. The dorsal portion of the spleen lies ventral to the vertebral end of the last rib and the first lumbar transverse process, on the left side of the body. The preferable point of penetration, therefore, is just posterior to the last rib close to the transverse process of the first lumbar vertebrae. In making a liver puncture a point close to the anterior border of the right twelfth rib, about two-thirds of the distance between the vertebral extremity and costochondral junction of this rib, is the best point of entry for the needle. When the puncture is made the animal should be well restrained in order to guard against tearing the organ through sudden movement.

It is not necessary to obtain blood from the organ to insure results, a small amount of the spleen or liver pulp being most desirable. On withdrawing the needle the material is blown out on a clean cover slip, allowed to dry, stained by Giemsa's or Leishman's methods, and examined microscopically for Leishmania.

Until recently, medical treatment of Leishmaniasis offered but little hope of success. Lately, however, in human medicine, good results have been obtained from intravenous injections of tartar emetic, extending the treatment over a period of several months, gradually increasing the dosage. While in exceptional cases attempts to rid dogs of the parasite by medicinal means might be justified, generally, animals proven to be carriers of Leishmania should be promptly destroyed.

As fleas are likely factors in the transmission of the infection, dogs and cats in localities where the disease is prevalent should be kept as free as possible from fleas.

C. CARRIERS OF FILTERABLE VIRUSES

1. The virus of foot-and-mouth disease

Foot-and-mouth disease or aphthous fever, caused by an ultramicroscopic, filterable virus, which up to the present time has not been artificially cultivated, is an important disease of cattle and other cloven-footed animals. The disease is prevalent in Europe, Asia, Africa and South America. At present it does not exist in the United States, the last and largest outbreak having occurred here in 1914–1915.

Loeffler, Hess, Zschokke, Bartolucci, Neverman and various other investigators have shown that cattle which have had foot-and-mouth disease often harbor the virus and are capable of infecting other animals for considerable periods following recovery. Just how long such animals may remain carriers has not been definitely ascertained. Cases are on record, however, in which it has been definitely demonstrated that some carriers are capable of spreading the infection 7 months after recovery from the disease.

Man not infrequently contracts foot-and-mouth disease. The infection is usually brought about through the ingestion of raw milk or cheese and butter prepared from milk containing the virus. Infrequently infection may occur as a result of direct contact with affected animals.

The disease in man commences with a slight fever, with nausea in some cases. The buccal mucous membranes become inflamed and vesicles, sometimes as large as peas, develop, especially on the lips, gums and cheeks. Vesicles may occasionally develop on the conjunctivae. Exanthema of the skin of the hands, particularly at the end of the fingers and at the base of the nails, occurs. Headaches, dullness, dizziness, abdominal cramps and diarrhea may be observed. The disease in adults usually runs a mild course. In children a severe gastro-intestinal catarrah is occasionally associated with the disease and may lead to fatal terminations.

Bussenius and Siegel (22) in recording 16 outbreaks of foot-and-mouth disease among animals, occurring between 1878 and 1896, report that entire families, and in several instances the great per-

centage of persons in certain townships, became affected with the disease. A total of 75 cases terminated fatally.

Thus, while the disease may be transmitted to the human species from animals suffering from the disease, until more definite knowledge is gained as to the various possible locations of the virus in the body of recovered animals which harbor the same, it will be impossible to state just how much of a menace carriers are to the health of man.

Habitat of the virus. As above indicated, studies of the carrier problem in foot-and-mouth disease, unfortunately, have not as yet established with certainty all possible places of abode of the filterable virus in the animal body.

Zschokke (23) demonstrated that vesicles, such as occur in the interdigital space, the plantar cushion and coronary band, may likewise be found between the horn and sensitive lamina of the hoof. Such vesicles may become confluent with the vesicles of the interdigital space or plantar cushion, thus opening to the outside, or they may remain separate. In the latter event the virus contained in the vesicles remains in such location long after the animal has recovered, and is brought to the surface by the natural wearing away of the hoof. The spread of foot-and-mouth disease by a carrier thus harboring the virus in the hoof, has also been reported by Bang (24).

It does not follow, of course, that the virus of foot-and-mouth disease is always localized in the hoofs of carriers. That it is probably harbored in other parts of the body and at times eliminated with the urine, feces, milk or saliva, is evident from the history of numerous outbreaks of the disease following the introduction of recovered animals into herds free of the infection.

Detection and management. Loeffler (25), in concluding his report on carriers of the virus of foot-and-mouth disease, stated that at that time there was no method known to distinguish virus carriers. The handicap resulting from inability to utilize bacteriological methods in the study of such carriers is, of course, obvious.

During the 1914–1915 outbreak of aphthous fever in the United States, the Bureau of Animal Industry of the United States Department of Agriculture (26) before releasing from quarantine the National Dairy Show Herd, the only herd of cattle affected

with the disease which was not destroyed, was confronted with the problem of definitely ascertaining whether or not any of these recovered animals were carriers of the virus. The disease had been eradicated from this country and a single carrier could, of course, have started the infection anew.

The recovered animals were maintained under the most rigid type of quarantine. A number of healthy young cattle, ranging from one to one and one-half years of age, were placed in contact with the recovered animals and were further subjected to various inoculation tests. In the exposure tests a susceptible animal was placed between two recovered animals and allowed to remain there forty-eight to sixty-four hours, after which time it was placed between two other recovered animals. This procedure was carried out until all recovered animals had been given an opportunity to infect the susceptible animals. The susceptible animals were rotated in this way three times so that each test animal was exposed at least one hundred and forty-four hours to each recovered case. In the meantime the recovered animals had been divided into groups and specimens of saliva, urine, vaginal discharge, watery extract of feces, scrapings from the interdigital spaces, and milk from each group were inoculated into the buccal cavity of the susceptible animals by rubbing the membranes briskly with a piece of gauze saturated with such specimens. Further, towards the end of the quarantine period a number of hogs were allowed to consume such leavings and droppings from the recovered cattle as had been permitted to remain, and were also fed milk from the cows.

These tests were continued over a period of seven months when the quarantine was lifted. They indicated that there were no carriers, capable of transmitting the disease, in this particular herd of recovered animals, which finding was subconsequentially borne out through failure of the released animals to infect others.

Numerous inoculation and exposure tests, as above outlined, to determine whether or not animals are carriers of the virus of foot-and-mouth disease, obviously, would not be practicable with individual animals, except in cases of breeding stock of considerable value.

As previously indicated, foot-and-mouth disease does not now exist in the United States and in the outbreaks that have occurred all infected herds, with the exception of the single instance noted, were promptly destroyed. Thus, in this country we have no carrier problem. However, in those localities where the disease exists, sanitary and quarantine measures must be relied on to minimize the spread of the infection by carriers.

With a view to eliminating all possibility of tranmission of the disease to man, through milk from cows which have recovered from the disease, the same should be properly pasteurized.

CHAPTER XVIII

Carriers of Organisms Pathogenic for Animals and Possibly for Man

A. CARRIERS OF BACTERIA

1. Streptococcus of infectious mastitis of cattle

Milch cows frequently suffer from mastitis as a result of infection with any one of a variety of bacteria. A streptococcus of the pyogenes type, however, is generally responsible for that form of the disease which is transmitted from animal to animal. Kitt, describing a streptococcus of bovine mastitis, referred to it as "Streptococcus agalactiae."

Cows which have apparently recovered from mastitis, and in some instances, cows with no history of having had the disease, often harbor streptococci in their udders for long periods of time.

Habitat of the organism. The udder may harbor and eliminate streptococci for several years. In those cases which have apparently not suffered an attack of mastitis, autopsy, as a rule, reveals no demonstrable changes in the udder tissue except, occasionally, a slight catarrhal thickening of the epithelium of the milk ducts. In cases with a history of having had the disease, however, remaining evidence of the attack is usually present in the form of fibrous tissue changes of varying degree, with atrophy of the alveolar structure of the parenchyma of the udder. A thickened condition of the epithelial lining of the milk ducts, from which the streptococcus may usually be isolated, is also a common finding in such carriers.

There has been considerable disagreement among various investigators as to the pathogenicity of streptococci of bovine origin for man. Some are of the opinion that man is readily susceptible to infection with bovine streptococci transmitted through milk from infected animals. The weight of evidence, however, stands in refutation of such conclusion. Generally, man possesses con-

siderable immunity to streptococci of bovine origin. Undoubtedly, however, streptococci of human origin occasionally gain entrance into the udder of cows through infected milkers, multiply in the glands, and may or may not set up pathological processes. Milk containing such organisms, is obviously dangerous as food for man unless pasteurized.

Detection and management. The organism can usually be isolated from the milk of carriers, by ordinary bacteriological methods, without difficulty. After the udder has been thoroughly washed with soap and water, followed by a 1:1000 solution of bichloride of mercury, and the operator's hands disinfected, the specimen of milk should be drawn direct into sterile containers and cultured with the least practical delay, icing the specimen if there will be appreciable loss of time in getting the same to the laboratory.

Our lack of accurate means for the definite identification of different types of streptococci applies, of course, in the case of the organism occurring in mastitis. The mastitis streptococcus must, however, be differentiated from Streptococcus lactis found normally in milk. Streptococcus lactis is characterized by its short chains of 3 or 4 organisms, some cells appearing elongated with tapering ends. When grown in litmus milk the color reduction precedes curdling and is complete. The mastitis streptococcus grows in long chains, and in litmus milk, causes curdling which may be followed by an incomplete reduction of the litmus.

The streptococcus usually enters the udder through the milk ducts, thus the transmission of the infection from the carrier to healthy cows is accomplished chiefly by the hands of the milker. Spread of the disease by this means can be controlled by requiring the milker to disinfect his hands after milking a known or suspected carrier.

Attempts have been made to eliminate the streptococcus from the udders of carriers through the injection of mild antiseptic solutions (10 per cent solution of argyrol, etc.) but the results, while worthy of trial, are not uniformly successful. Autogenous bacterins have also been employed with variable results.

A number of carriers of the organism suffer recurrences of the disease. Such cows usually develop marked udder changes with

great impairment of the functional activity of the gland. Thus, in addition to being carriers of the infection, they are a loss as milch cows, and unless they have a distinct breeding value, should be "beefed." Milk from herds in which there are known carriers of streptococci capable of producing mastitis in cows, should be pasteurized, in order to eliminate all chance of it proving detrimental to the health of man.

2. *Bacterium abortus* (*Bang*)

Of all infectious diseases of animals, bovine infectious abortion, caused by Bacterium abortus (Bang), is probably without an equal in importance from the standpoint of carriers. When it is realized that from an economic standpoint infectious abortion of cattle in the United States is second only to tuberculosis, and that carriers are very potent factors in its spread, their importance cannot be over-rated. According to Schroeder (27) 60 per cent of all infected cows at some time harbor Bacterium abortus in their udders.

While up to the present time this organism has never been definitely demonstrated to be pathogenic for man, nevertheless, it is possible that in specific instances and under certain conditions, this bacterium which is capable of producing marked lesions of a grave nature in various experimental animals, may prove detrimental to human beings consuming milk from carriers of the organism.

Mohler and Traum (28) inoculated emulsions of 56 tonsils and adenoids from children into guinea pigs and produced lesions in the liver, spleen and testicles in one of the inoculated pigs. Bacterium abortus was recovered from these lesions. Larsen and Sedgwick (29) submitted blood specimens from 425 children to the complement-fixation test for Bacterium abortus infection and obtained 73 positive reactions. Later work by these investigators with blood serum from 42 new-born babies who had not received cows' milk resulted in negative reaction to the serological test. Larsen and Sedgwick indicated that these reactions might possibly be due to a passive immunity resulting from the ingestion of milk containing antibodies. Later work along this line by Cooledge

(30) tends to indicate that these reactions are generally due to the absorption of antibodies contained in infected milk.

Habitat of the organism. Bacterium abortus has a particular affinity for embryonic tissue, its natural habitat being the epithelium of the chorion. In infected cows it is practically always found in the uterus during pregnancy, even though the animal goes through the full period of gestation and has an apparently normal parturition. After parturition, however, the organism soon disappears from the uterus; usually within several weeks. In exceptional cases it may persist for one and one-half to two months.

In the absence of embryonic tissue Bacterium abortus finds the udder a suitable place to maintain its existence. Thus in a large percentage of infected cows the abortion organism is harbored in one or more quarters of the udder and may be eliminated with the milk for periods varying from a few weeks to six or seven years. Up to the present time it has not been established that udder lesions, definitely attributable to Bacterium abortus, occur in cows carrying the organism.

The organism remains localized in the udder during the non-pregnant state in the cow but readily invades the uterus through the blood stream during pregnancy. Thus, the udder, in addition to eliminating the infection to the outside more or less continuously, constitutes a focal source of infection from which the uterus of its host may be reinfected when conditions there are favorable.

In addition to the cow, the bull may harbor and eliminate Bacterium abortus with his seminal fluid. Buck, Creech and Ladson (31) in an examination of 325 mature bulls, isolated Bacterium abortus from the vesiculæ seminalis in four instances. The organism in the bull apparently shows predilection for the seminal vesicles although it has been found in other parts of the reproductive organs.

Detection and management. In the detection of carriers of Bacterium abortus among cows and bulls, the agglutination or complement-fixation test should be resorted to, and this followed, in the case of cows, by bacteriological examinations of the milk from each quarter of the udder. In bulls, when practicable to obtain specimens of the seminal fluid, the same should likewise be

subjected to bacteriological examination. Because of its relative simplicity, the agglutination test is the preferable of the serological tests. In reliability for this work, it compares favorably with the complement-fixation test.

In applying the agglutination test either blood or milk serum from the suspected animal may be used. Blood serum, however, is preferable because in positive cases it usually possesses a greater number of agglutinins. In interpreting the agglutination test the lowest dilution in which agglutination is obtained which should be considered positive, has not been definitely settled. Agglutination in a dilution of 1 to 50 or greater, however, should be taken to indicate that the animal is then, or was at some time previously, infected with Bacterium abortus. If positive reactions are obtained with serum in dilutions of 1 to 50 or greater but in less than 1:200, the animals should be isolated and the agglutination test repeated after three week intervals. Declining reactions in dilutions below 1:200 can be taken, with a reasonable degree of certainty, to indicate that the animal is not a disseminator of Bacterium abortus. Schroeder (27) in speaking of the work of the United States Bureau of Animal Industry and other investigators with the agglutination test for infectious abortion, states that where it can be proven that a cow harbors Bacterium abortus in her udder, the agglutination reaction obtained with blood or milk serum will be positive in a dilution of 1:200 or more.

In the bacteriological examination of milk to detect carriers of Bacterium abortus, Huddleson (32) recommends a liver infusion agar, prepared without excessive heating and filtered through glass wool rather than cotton or paper, and with a H-ion concentration between 6.6 and 6.4. One part of a saturated aqueous solution of gentian violet to 10,000 parts of this medium will inhibit the growth of a large percentage of organisms other than Bacterium abortus. The inoculated plates should be incubated at 37.5°C. in air-tight containers in which approximately 10 per cent of the air has been replaced by CO_2 gas, an increased carbon dioxide tension being essential to the initial growth of Bacterium abortus.

Cows and bulls demonstrated to be carriers of Bacterium abortus should not be introduced into uninfected herds. The ideal method of control, would, of course, be the slaughter of all cattle reacting

to the agglutination test followed by thorough disinfection of the premises and subsequent retests of remaining animals. In herds of pure-bred animals, or where the infection is limited and of recent introduction, such method might be most economic.

While this radical method might prove the most economic procedure in some instances, generally, in herds where the disease is well established, and in which there is a high percentage of carriers, it would not be feasible. The situation in such cases can probably best be handled by maintaining the herd intact without introducing new animals into it and without permitting animals from it to be introduced into other herds. Thus, while carriers in such herds will not be eliminated they are among animals which have developed more or less immunity to the infection and consequently are in the place where they will do the least harm, especially where energetic sanitary measures are employed with a view to preventing mass infection.

The bull, known to harbor and eliminate Bacterium abortus, under average conditions apparently does not infect healthy cows through the vagina. Infection from such animal is usually brought about through the ingestion of food or water contaminated with semen dripping from the penis of the bull or which has escaped from the vagina of the cow subsequent to service. Thus where such carriers are utilized for breeding purposes, precautions should be taken to prevent the spread of the infection in this manner. On the other hand, it appears possible that under certain unusual conditions, especially in cases of slight injury occurring during service, cows may become infected through the vagina when served by bulls known to carry and eliminate the organism. It cannot, therefore, be definitely stated that such carriers are invariably safe for breeding purposes.

Although possible pathogenicity of Bacterium abortus for man has not been established, pasteurization of milk from herds in which there are carriers is fully warranted.

B. CARRIERS OF PROTOZOA

1. Trypanosomes

There are several important diseases of domestic animals, known to be due to trypanosomes. Further, a very large variety

of trypanosomes of little or no established pathogenicity have been noted in numerous species of lower animals.

Of the more important diseases of animals due to trypanosomes there are four which are outstanding. Nagana, an acute or chronic affection of solipeds, cattle, sheep, goats and other ruminants, caused by Trypanosoma Brucei, at present exists in Southeast Africa. The disease is characterized by remittent fever, subcutaneous edema, marked anemia and emaciation. It is transmitted by the tsetse fly.

Surra, designates those trypanosomiases of domestic animals caused by Trypanosoma Evansi. The disease causes great losses among solipeds and camels. Cattle and dogs are less severely affected. Surra occurs in India, Persia, China, the Philippines, Sumatra, Java, Mauritius, and apparently in northeastern Africa. Its manifestations are in a general way similar to those of nagana. Tropical flies, especially Tabanus tropicus and Tabanus lineola, are transmitting agents of the disease.

Dourine, caused by Trypanosoma equiperdum, is a chronic disease of horses, characterized by inflammatory swelling of the external genitals with subsequent symptoms of paralysis. The disease at present appears to exist in Spain, Russia, Africa, Persia, India, Java, Roumania, France and in several states in the United States. Characteristic of dourine is the fact that the natural mode of infection is through coitus.

Mal de caderas, caused by Trypanosoma equinum, is a fatal subacute or chronic disease of horses in South America, characterized by a paralysis of the hind quarters. Definite information is lacking as to the natural mode of infection. It is believed, however, that flies are capable of transmitting the disease.

There are numerous records of carriers of trypanosomes pathogenic for animals, especially Trypanosoma Brucei and Evansi. According to Laveran and Mesnil (33) a large variety of species, particularly wild ruminants, harbor Trypanosoma Brucei in their blood without suffering impairment of health. Hutyra and Marek (34) report buffaloes, antelopes, hyenas, zebras and quaggas as carriers of the organism, such animals themselves being refractory to the infection.

In surra the bovine species is much more resistant to the disease than equines. However, cattle and zebus in localities where the

disease exists are very frequently carriers of the trypanosome. Such animals may harbor the organism for years without manifesting disturbances of health. Camels which have recovered from surra frequently harbor Trypanosoma Evansi in their blood for long periods of time. In India the buffalo has been demonstrated as a frequent carrier of the parasite. Various wild animals such as foxes, jackals, hyenas, etc., may carry the organism.

In dourine animals which have made an apparent recovery may continue to harbor the parasite in their bodies for a considerable period of time as is evidenced by relapses which frequently occur in such animals.

Nothing definite is known regarding carriers in Mal de caderas. It has not been definitely established that trypanosomes pathogenic for man are, under natural conditions, carried by lower animals. However, Trypanosoma gambiense, the causative agent of so-called "sleeping sickness" in man has been experimentally demonstrated to be pathogenic for various species of animals, horses, cattle, sheep, monkeys, dogs, cats, rats and mice having been successfully infected.

Bruce (35) and his co-workers were able to transmit Trypanosoma gambiense from infected monkeys to cattle by the bite of Glossina palpalis. They expressed the opinion that cattle may harbor the parasite. Thomas and Brienl (36) inoculated a cow with Trypanosoma gambiense and noted that it suffered a slight disturbance of health but soon returned to normal. More than a year later the blood of this animal was still infectious for rats.

Habitat of the organism. With the exception of Trypanosoma equiperdum, the trypanosomes above mentioned, when harbored by animals, are present more or less intermittently in the blood stream. At periods they undoubtedly inhabit various tissues and organs when they cannot be demonstrated in the circulating blood.

In dourine the trypanosome can, only in the rarest instances, be demonstrated in the blood of animals harboring the organism within their bodies. Recurrence of symptoms of the disease and positive serological reactions constitute the evidence that such animals actually harbor the infection.

Detection and management. Microscopic examination of blood preparations from animals suspected of harboring trypanosomes

may be resorted to with successful results in a number of positive cases. However, such examination frequently results in failure to demonstrate the parasite. Animal inoculation tests often give positive results where the microscopic examination fails.

The complement-fixation test has proven of great value in the detection of dourine among horses in the United States, and the same test can be used to good advantage in the detection of carriers of trypanosomes. However, the complement-fixation test will not differentiate the type of trypanosome, the phenomena being a group reaction. Thus, while carriers may be detected by the serological test, identification of the type of organism harbored can only be accomplished where it is possible to demonstrate and definitely recognize the particular parasite microscopically, or where the typical disease can be produced as a result of experimental inoculation of susceptible animals.

When carriers of pathogenic trypanosomes are detected in localities where trypanosomiasis is not prevalent, their destruction should be accomplished. In districts where the disease is widespread, however, measures looking to the protection of animals from flies, must be chiefly relied upon to combat the carrier problem. In cases of animals harboring the dourine trypanosome, the problem can be effectively handled by castrating stallions known to harbor the organism and prohibiting the breeding of infected mares, or destroying the latter in countries where efforts are being made to eradicate the disease.

2. Other protozoal and metazoal infections

There is evidence tending to indicate that different species of animals may occasionally carry in their intestinal tracts various rhizopoda, ciliata, flagellata and sporozoa, in small numbers without manifesting disturbances of health. Again, it is possible that certain of such parasites may be harbored in rather large numbers by a particular species without detrimental results, whereas the same organism gaining entrance into the body of other species, including man, may cause marked disturbances. At the present time, however, there is very little known regarding carriers of this type.

Eichhorn and Gallagher (37), in reporting an outbreak of amebic dysentery among monkeys, point out the possibility of carriers occurring among such animals. The parasite in the cases described, however, apparently was not Endameba histolytica, the causative agent of amebic dysentery in man.

Adult turkeys may harbor in their intestines Ameba meleagridis, the etiological factor in infectious enterohepatitis ("Blackhead") of turkeys. Apparently this parasite is also carried by chickens. There is no evidence that the organism is pathogenic for man.

Balantidium coli is commonly found in the lower portion of the intestines of hogs. It is usually nonpathogenic for these animals but may occasionally produce a mild form of dysentery. This organism is capable of producing dysentery and ulceration of the intestines in man, occasionally setting up a process which terminates in death.

Several types of trichomonas occur in swine and fowls. So far as is known, however, they are of but little importance.

Various coccidia occur in cattle, sheep, dogs, cats, rabbits, fowls, etc. Undoubtedly there exists among such animals those which could be properly placed in the category of carriers. There is, however, but little information available on the subject. There are several cases on record where man has been infected with Coccidium cuniculi, the common coccidium of rabbits.

In the same sense that carriers of protozoan organisms are recognized, carriers of various types of helminths exist among animals. Our knowledge of this phase of the carrier problem, however, is very meagre.

CHAPTER XIX

Carriers of Organisms Pathogenic for Lower Animals Only

A. CARRIERS OF BACTERIA

1. Bacillus bipolaris septicus

Bacillus bipolaris septicus, various types of which make up the "Hemorrhagic Septicemia" or "Pasteurella" group and are known as B. bovisepticus, B. equisepticus, B. suisepticus, B. ovisepticus, B. avisepticus, etc., according to the species of animal from which isolated, is frequently harbored in the bodies of normal animals.

According to Moore (38), upward of 80 per cent of normal cattle harbor in their upper air passages organisms corresponding in cultural characteristics, and in their effect upon rabbits, to Bacillus bipolaris septicus. Horses, swine, sheep, dogs, cats and fowls have also frequently been found as carriers of the organism.

Fortunately, this bacillus is usually more or less of a facultative-pathogenic organism and only produces its specific disease when the normal resistance of the invaded animal is lowered or following a particular increase in its own virulence which sometimes occurs without apparent cause.

Habitat of the organism. The favorite location of Bacillus bipolaris septicus in carriers apparently is the epithelium of the nasal cavity, larynx, pharynx and trachea. It is also found relatively frequent in the small and large intestines.

Manninger (39) cites an experiment in which chickens were artificially infected with the fowl cholera organism (B. avisepticus) and, while not developing the disease, eliminated the organism through their kidneys for months. He also cites an instance of a hen harboring highly virulent fowl cholera organisms in an old encapsulated abscess in the region of a joint in which she had a chronic arthritis.

No tissue alterations, commonly found, and definitely attributable to this organism when harbored by apparently normal animals, have been described.

Detection and management. The organism can, as a rule, be readily cultivated from the upper air passages of carriers by ordinary bacteriological methods, and when carried in the intestinal tract, may likewise be isolated from the feces, but with less frequency.

Because of the high percentage of carriers and the widespread distribution of organism of the Pasteurella group in nature, we are without means for eliminating them. Efforts, therefore, must be directed along sanitary lines with a view to maintaining the general health and resistance of animals, rather than endeavoring to eliminate the carriers. Further, vaccination against infection with organisms of this group, with properly prepared vaccines, is possibly of value.

2. Bacillus necrophorus

Bacillus necrophorus (Flügge) under this and such additional names as "Bacillus diphtheriae vitulorum" (Loeffler), "Bacillus filiformis" (Schütz), "Actinomyces cuniculi" (Gasperini), and "Streptothrix necrophora" (Kitt), since 1884 has been recognized as the causative factor of a variety of important pathological processes in domestic animals. The organism is widely distributed and is frequently harbored in the intestines of healthy herbivorous animals, especially hogs. There is no record of its having proved pathogenic for man.

The principal pathological conditions for which bacillus necrophorus is responsible includes gangrenous dermatitis of horses and mules, the so-called "foot-rot" and "lip-and-leg ulceration" of sheep, necrotic stomatitis of cattle, and multiple necrotic foci in the liver of cattle and hogs. The organism is also found as a secondary factor in various other diseases and conditions. Its lesions are characterized by a coagulation necrosis with subsequent caseation.

In the United States Army during the world war, gangrenous dermatitis of horses and mules proved to be the second most important disease of animals in the United States. During the

six month period July to December, 1918, 4036 cases of the disease were reported. Of this total 212 cases died or had to be destroyed on account of the disease. Of all deaths, from all causes, among all Army animals in the United States, for this period 6.41 per cent were due to gangrenous dermatitis. The weekly sick report during this period showed a ratio of over 275 animals per 1000 on sick report as a result of Bacillus necrophorus infection.

Where a considerable number of animals are kept together in corrals, pens, lots, etc., which are wet and muddy, or contain large accumulations of manure, the infection spreads rapidly when once introduced. The importance of carriers when placed among animals in such surroundings is obvious.

Habitat of the organism. Carriers of Bacillus necrophorus harbor the organism in their intestinal tracts, usually without manifesting appreciable lesions However, in hogs which have had the chronic form of hog cholera, Bacillus necrophorus is frequently found associated with Bacillus suipestifer in the intestinal ulcers described in the discussion of carriers of the Salmonella group (page 131). Further, the organism may be found in minor intestinal lesions originally due to parasites.

Detection and management. The detection of Bacillus necrophorus in carriers by bacteriological methods is by no means an easy undertaking. In the first place, carriers of this bacillus as a rule do not eliminate it in large numbers. Further, this organism is an extremely difficult anaerobe to isolate in pure culture. Characteristic of the organism is its beaded appearance in stained preparations. While it is distinctly a pleomorphic organism, it usually occurs as a long slender rod appearing more or less bent. Long filaments, measuring in some instances, over 100 microns in length, are frequently observed.

The subcutaneous inoculation of rabbits with suspected material gives rise in positive cases to a hard inflammatory induration at the site of inoculation. After a few days the tissue in this area becomes caseous and necrotic, the rabbit usually dying within 10 or 12 days. The necrotic tissue gives off a characteristic cheesy odor. In such lesions B. necrophorus can be demonstrated in large numbers.

Sanitary measures afford the chief means of preventing B. necrophorus infections. Well drained corrals, pens, etc., and proper disposal of manure and litter are potent factors in controlling the infection.

3. Bacillus paratuberculosis

Paratuberculous enteritis, or Johne's Disease, is a serious, chronic, infectious disease of the bovine species, characterized by a marked thickening and corrugation of the mucous membrane of the intestine. The etiological factor, Bacillus paratuberculosis, is an acid-fast organism closely resembling the tubercle bacillus.

Young cattle are more resistant to the infection than adults, yet they are capable of carrying the infection for months or even several years, and therefore constitute an important carrier problem. After maturity, a large percentage of such carriers themselves become affected with the disease, especially following calving.

While the disease in the vast number of cases runs a long chronic course and terminates fatally, there are, among adult cattle, occasionally cases of apparent recovery. Such animals invariably are active carriers of the infection, in some instances for periods of time extending over a number of months. Usually, however, they suffer recurrences which finally result in death. Such animals must be differentiated from the true immune carrier, as generally they are, in a strict sense, arrested cases, the carrier state existing during the period of inactivity.

Habitat of the organism Carriers of the bacillus of paratuberculous enteritis harbor the organism in the mucous membrane of the small and large intestine, the lower portion of the small intestine being a favorite location.

In the case of young cattle which, while carrying the organism, have not suffered an attack of the disease, autopsy reveals little or no changes in the intestinal tract. Occasionally, however, small areas of the intestinal mucous membrane may appear thickened and slightly rugous. Sections from such areas show, principally, cellular infiltration and a swollen and more or less distorted condition of the villi. The organism can readily be demonstrated in such lesions.

In carriers which have had the disease the mucous membrane of portions of the intestines appears, as a rule, greatly thickened and has a characteristic convoluted or corrugated appearance. Microscopic examination of sections of such tissue reveals a cellular infiltration, a marked distorted condition of the villi, and an increase of the interstitial tissue between the tubular glands in the glandular layer, with atrophy of the glands. In such sections the acid-fast bacillus can usually be demonstrated in considerable numbers.

Detection and management. Microscopical examination of the feces from actual carriers often yield negative results. Repeated examinations of considerable quantities of the feces should, therefore, be made. Further, the bacillus of Johne's disease must be differentiated from other acid-fast organisms. As it is nonpathogenic for the guinea pig, such experimental animal can be utilized in differentiating the organism from the tubercle bacillus. It must, however, still be differentiated from acid-fast organisms of a saprophytic nature. As it is exceedingly difficult to cultivate the Bacillus paratuberculosis, cultural methods, at present, offer but little aid. Hastings, Beach and Hadley (40) report fairly good results with a medium prepared by adding to filtered broth cultures of the human tubercle bacillus sterilized in the Arnold sterilizer for two hours, 15 grams of agar, 2 grams of beef extract, 5 grams of peptone, 2.5 grams of potassium acid phosphate and 24 cc. of glycerine, per liter of the filtered culture, adjusting the reaction to plus 1.5 to phenolphthalein. A small amount of sterile blood serum should be run over the surface of this medium just before inoculation.

Bang (41) and several other investigators have called attention to the value of avian tuberculin for the diagnosis of paratuberculous enteritis. Tuberculin prepared from the avian type of tubercle bacillus is utilized in order to eliminate the possibility of complications arising from reactions in tuberculous cows, animals infected with the bovine or human type of tubercle bacillus not reacting to avian tuberculin. Such tuberculin test may be used in the detection of carriers.

A diagnostic agent ("Johnin") prepared similarly to tuberculin but from the specific organism of the disease has been made and

gives satisfactory results in diagnosing the infection. However, because of the difficulty encountered in propagating the bacillus it is but seldom that such agent can be obtained.

As Johne's disease is fatal in the large percentage of cases, and as carriers, as a rule, eventually develop the disease, or if they have already had it, suffer recurrences which finally prove fatal, they should be slaughtered.

4. Bacterium pullorum

The carrier problem in bacillary white diarrhea of young chicks, a disease due to an organism known as Bacterium pullorum, is without doubt the most important problem of its kind in the various infectious diseases of fowls. Gage (42), Jones (43), Rettger (44), and various other investigators, have definitely shown that the perpetuation of this disease is due, in a large measure, to carriers of the organism among adult hens, who may harbor the organism throughout their life.

The organism is apparently non-pathogenic for man. This is a fortunate circumstance in view of the fact that the bacterium is frequently found in freshly laid eggs of carriers.

Habitat of the organism. Carriers of Bacterium pullorum harbor the same in their ovaries. The changes in such ovaries are usually well marked. Examination of a normal ovary of the laying hen demonstrates a large mass of ova in various stages of development, some appearing as minute, colorless spheres, just visible to the naked eye, others being as large as a normal yolk and of a rich yellow color. The ovary which is infected with Bacterium pullorum, while possessing some apparently normal ova in various stages of development, will usually be found to contain a number of different sizes which appear as cysts. The smaller of such ova appear round or are slightly distorted. The larger are usually distorted so that they appear angular or flattened, and are of a mottled appearance, some lighter than normal, others of a dark, yellowish-brown color. In some cases the color is a peculiar dark-green, suggesting gangrene. The diseased ova contain a cheesy mass out of which may be expressed a clear amber-colored fluid. Bacterium pullorum may be readily isolated from such material.

A large percentage of ova of hens with such ovaries never mature. However, such birds frequently lay fully developed eggs, capable of hatching, which contain the organism. In such cases the resulting chick has white diarrhea and infects others in the brood which may have been hatched from healthy eggs. Of those that survive a large percentage of the females are carriers, thus continuing the cycle of infection.

Rettger, Kirkpatrick and Jones (44) in a series of experiments which they conducted found that over 25 per cent of female chicks infected with Bact. pullorum when small became permanent carriers of the infection.

Detection and management. Jones (43) found that the macroscopic agglutination test could be utilized to good advantage in detecting hens harboring Bact. pullorum in their ovaries. The value of this test has been confirmed by a number of other investigators.

In carrying out the agglutination test dilutions of 1:50, 1:100 and 1:200 are made. In Jones' work serum from all infected fowls agglutinated in 1:50 and 1:100 dilutions, 91 per cent agglutinated in the 1:200 dilutions and 82 per cent of 1:500. Agglutination in dilutions of 1:100 or more should be considered positive, in the 1:50 dilution, suspicious.

Hens demonstrated to be carriers of Bact. pullorum should not be kept on premises where chickens are raised. Further, because of the diseased condition of the ovaries, such birds are not profitable layers. Therefore, their slaughter for food purposes is an economical procedure.

B. CARRIERS OF PROTOZOA

1. Piroplasma bigeminum and Piroplasma bovis

In the southern part of the United States bovine piroplasmosis or Texas fever is an important disease of cattle. It is caused by Piroplasma bigeminum and is commonly transmitted by the tick Margarapus annulatus. European piroplasmosis (British "Red Water") is generally due to a smaller type of organism, Piroplasma bovis, and is usually transmitted by Ixodes ricinus. Clinically, Texas fever and European piroplasmosis of cattle are practically

indistinguishable. However, cattle immune to the Texas fever piroplasma are susceptible to the European type, thus clearly establishing that the two parasites are different species.

Young cattle are quite resistant to piroplasma infection. Animals raised in infected localities usually become immunized so that they do not suffer from severe attacks of the disease. Such animals, however, harbor the piroplasma and if introduced into districts where piroplasmosis does not exist, prove a source of infection for susceptible cattle if transmitting ticks are present.

Piroplasma may persist for years in the blood of immune or recovered animals. Schroeder and Cotton (45) reported the case of a cow whose blood was infectious for over 10 years subsequent to her arrival at the United States Department of Agriculture Experiment Station from a Texas fever district in North Carolina.

Habitat of the organism. Carriers of Piroplasma bigeminum and Piroplasma bovis harbor the same in their red blood corpuscles. Piroplasmosis is characterized by a marked diminution of red cells. After recovery, however, the number of red cells gradually approach normal so that in carriers blood cell counts often demonstrate little or no diminution.

Detection and management. The parasites of bovine piroplasmosis may be demonstrated in the blood of carriers by microscopic examination. They are present, of course, in smaller numbers than are found in cases of the disease, consequently a more searching examination is often necessary.

After shaving and cleaning an area of the ear of a suspected carrier a drop of blood should be obtained by making a small incision with a scalpel or lancet. A blood film should be prepared on a clean slide and stained for microscopic examination with Romanowski stain or one of its modifications. Piroplasma bigeminum appear as pyriform organisms varying from 2.0 to 4.0 microns in length and 1.5 to 2.0 microns broad, usually occurring in pairs in the red blood cells. They may be found side by side but frequently appear end to end on a parallel line or at an angle, the pointed ends being in opposition (dumb-bell forms). In addition to the pear-shaped forms, round, oval or pyramidal shapes may be noted. Occasionally but one parasite may be found in a cell while in other cells several pairs may be noted. Piroplasma

bovis differs from Piroplasma bigeminum in that it is smaller and does not have the tendency to occur in distinct pear-shaped forms.

As bovine piroplasmosis is transmitted from animal to animal by certain species of ticks, preventative measures, in the United States, have been reduced to quarantine of areas infected with the cattle tick and the inauguration of a well-organized campaign of tick eradication. Cattle from such districts cannot be shipped into uninfected territory except under certain restricted conditions. Between 1906 (the year eradication of the cattle tick was undertaken) and December 1921, 523,837 square miles of infected territory in the United States were freed of cattle ticks through systematic dipping of the cattle, reducing the infected area to 206,015 square miles.

In localities where bovine piroplasmosis is more or less wide-spread, and where quarantine and measures for the eradication of transmitting ticks are not employed, the immunization of susceptible animals constitutes the only means of protecting cattle from infection coming from carriers. This is accomplished naturally in young animals brought up in infected districts. Susceptible adults may be immunized through the subcutaneous injection of small amounts (5 cc.) of defibrinated blood of immunized or recovered cattle, preferably calves, in which the parasite occurs in small numbers. The inoculated animals should be kept in the stable for three or four weeks before being turned out to pasture. Eight to ten days after the inoculation the animals manifest symptoms of the disease which usually last from one to two weeks. Pregnant cows and animals in a state of impaired health should not be inoculated.

Most inoculated animals survive the infection, although occasionally a few are lost. However, as the percentage of losses among non-inoculated animals, in localities where the disease is wide-spread, is considerably greater than that occurring in artificially infected animals, the inoculation procedure is warranted.

Where vaccination is employed to immunize susceptible animals, we have, so far as the carrier problem goes, a unique situation. The method employed to protect non-immunes against infection actually produces a large number of carriers.

2. Piroplasma caballi and Nuttallia equi

Prior to 1910, Piroplasma caballi, Piroplasma equi or Babesia equi, as it has been variously termed, was the single etiological entity considered in connection with equine piroplasmosis. In 1910, however, Nuttall and Strickland (46) reported the rosette or cross-form type of organism, which had previously been considered merely a form of Piroplasma caballi, as a distinct and separate type of blood parasite and termed it "Nuttallia equi."

At present the findings of Nuttall and Strickland are generally accepted and two types of organism recognized. However, as mixed infections are not of rare occurrence, and as it has been practically impossible to differentiate clinically the disease induced by these two types of organism, no attempt has been made to separate the two affections. Thus, the term "equine piroplasmosis" includes those diseases caused by either one or both of the organisms mentioned.

Equine piroplasmosis is of frequent occurrence in Russia, Italy, Africa and India. While it is not known to exist in the continental United States, it has been recognized on the Canal Zone.

Horses which have recovered from the disease may harbor the organism in their blood for years and through the agency of ticks (the natural mode of infection) infect healthy animals.

Habitat of the organism. Carriers of Piroplasma caballi and Nuttallia equi harbor the parasites in some of their red blood corpuscles. The number of red cells which may be found to contain the organisms, however, is exceedingly small as compared to that in actual cases of the disease.

Detection and management. Carriers of Piroplasma caballi and Nuttallia equi may be detected through microscopic examination of stained blood-smear preparations from such animals. It is often necessary, however, to examine a large number of preparations at different periods before the organism can be demonstrated.

Piroplasma caballi represents the true type of Piroplasma and resembles, rather closely, Piroplasma bigeminum, the causative agent of Texas fever in cattle. It appears as a relatively large, elongated or pyriform body, averaging approximately 3 to 3.5 microns in length and is usually found in the red blood cell in pairs or singly.

Nuttallia equi is considerably smaller than Piroplasma caballi and is characterized by its occurrence in rosette or cross-forms, four parasites being thus grouped. Occasionally there may be observed small ring-like or coccus forms of the Nuttallia.

At present there is no known medicinal agent which has given satisfactory results in eliminating these organisms from the blood stream. Thus, in countries or localities where equine piroplasmosis has not become established the detection of a carrier of the infection would call for its immediate destruction. In communities where the disease is prevalent, however, such procedure would not be feasible, especially when it is considered that a vast number of animals in such places are carriers of the organisms. In these localities only young native animals become affected, the older horses, mules and donkeys having more or less of an acquired immunity, develop the disease or suffer a relapse if they have previously had the affection, only under conditions which tend to lower their normal resistance.

Susceptible animals should be kept from tick-infested pastures, especially during the warm months when ticks are numerous. The vaccination of susceptible animals according to the method recommended by Theiler demonstrated that passage of the organism through donkey colts reduces the virulence of the parasite, especially for horses who are more susceptible to the disease than mules and donkeys. In carrying out the vaccination of susceptible animals, blood containing parasites which have been passed through 4 or more donkey colts, is used as the inoculum. Susceptible animals are injected with 1 cc. of such blood. Such inoculation gives rise to but a minor reaction. Pregnant mares and animals in poor condition should not be vaccinated. As in bovine piroplasmosis, vaccination actually produces a large number of carriers.

C. CARRIERS OF FILTERABLE VIRUSES

1. The virus of equine infectious anemia

Equine infectious anemia, manifesting itself as an acute or chronic, septicemic affection with marked destruction of red blood corpuscles, is one of those diseases of horses caused by an ultra-

microscopic filterable virus, in which carriers are recognized. The malady is prevalent in several of the European countries, in Canada, and in the United States has been recognized in Minnesota, South Dakota, Nebraska, Nevada, Kansas, New York, Virginia and Texas. It is undoubtedly more widespread than is generally believed.

In practically all instances the disease eventually has a fatal termination. Animals which have the chronic form of the affection sometimes make an apparent recovery, continuing in health for months or even years. Almost without exception, however, they suffer relapses which finally terminate fatally. Such apparently recovered horses are "relapsing carriers." They continue to harbor the virus in their bodies and through its elimination in the urine, are a menace to the health of other animals.

Habitat of the virus. The virus of equine infectious anemia is present in the blood stream of carriers and is eliminated more or less continuously in the urine.

The blood findings in infectious anemia vary with improvement of the animal, so that usually in carriers which have apparently recovered, the shortage of red corpuscles is very moderate as compared with the marked diminution (10 to 25 or even 50 per cent) of blood cells in active cases.

Detection and management. Positive identification of carriers of the virus of infectious anemia can only be made through the inoculation of normal horses with blood specimens from suspected carriers. In positive cases a test horse given an intravenous inoculation of 25 to 50 cc. of blood or blood serum (the particular amount apparently has no effect on the incubation period) usually develops the disease within eight or nine days, although in rare instances two or three weeks may elapse before the development of symptoms. In some cases such test animals may die within two or three weeks after the development of symptoms. Again they may develop the chronic type of the disease in the very beginning. Such cases run a rather long course before developing more manifest symptoms of the disease than periodical rises in temperature.

When obtainable, a definite history of a previous attack of infectious anemia in a suspected carrier, is, for practical purposes, sufficient to incriminate the animal.

In view of the fact that carriers of the virus of infectious anemia, besides menacing the health of other horses, almost invariably suffer relapses which finally terminate fatally, they should be promptly destroyed and the carcasses properly disposed of.

2. The virus of contagious pleuro-pneumonia of cattle ("Asterococcus mycoides")

Contagious pleuro-pneumonia of cattle is an acute, subacute, and occasionally chronic, disease of cattle, characterized by exudative inflammation of the interlobular lymph vessels and alveolar tissue of the lungs, with a sero-fibrinous pleurisy.

The disease at present does not exist in the United States, the last case in this country being destroyed in 1892. This scourge, however, has made its appearance in the United States several times and has been eradicated only through energetic efforts of the federal Department of Agriculture in coöperation with the authorities in the states involved. During 1886, in the state of Illinois alone, approximately 10,000 cattle were affected with the disease.

Contagious pleuro-pneumonia is caused by a very minute virus which will pass the Berkefeld filter and the Chamberland cylinder of "F" porosity, but is held back by the Chamberland "B" filter. It is possible to cultivate the organism artificially in Martin's bouillon containing beef serum, and also in several other types of serum media. When magnified approximately 1500 diameters with considerable illumination, the organisms are seen as polymorphic bodies, appearing as minute refracting dots, very short spirillae, and branching and asteroid figures. Borrel (47) and his associates in studying the pleomorphic nature of the organism observed coccic, streptococcic and morula-shaped forms, as well as short, spiral threads, showing fork-shaped branchings, and asteroid and mycelioid bodies, surrounded with a fine mucin covering. Because of these findings he termed the organism "Asterococcus mycoides."

Animals which have apparently recovered from contagious pleuro-pneumonia have been known to harbor and transmit the virus to healthy animals several months to two or three years subsequently. The great percentage of such recoveries, however, are more apparent than real as relapses in arrested cases usually

occur. The majority of these carriers, therefore, come in the category of "relapsing carriers."

Habitat of the virus. The virus of contagious pleuro-pneumonia is usually found in sequestrated and encapsulated lesions in the lungs of animals which harbor the infection following apparent recovery.

Autopsy of such animals reveals in one or both lungs, a single, rarely several, so-called "sequesters." In these lesions areas of the lobular tissue have undergone necrosis. The necrotic portion is surrounded by a dense connective tissue capsule, the necrotic piece lying free (occasionally partly adherent) in the cavity thus formed. This necrotic piece, in cases which are not of too long standing, consists of a soft, mushy, outer portion and a rather firm inner part, which on section appears mottled. In long-standing cases this tissue breaks down, forming a thick, greasy, pasty mass. When such lesions are comparatively small they may gradually become absorbed. In a large percentage of cases, however, the process subsequently breaks through the limiting capsule, giving rise to a recurrence of the acute condition, with spread of the infection. When these "sequesters" are entirely closed by the connective tissue capsule the virus in the lesion is held in such locality. However, when they communicate with a bronchus infectious material is more or less continuously expelled.

The circulating blood is not favorable for the propagation of the virus of contagious pleuro-pneumonia, hence, in carriers, it is not harbored in the blood stream.

Detection and management. Detection of carriers of the virus of contagious pleuro-pneumonia is practically impossible of accomplishment through examination of the suspected animal in the living state. History of cases of the disease associated with certain animals, and knowledge of previous pulmonary affections in suspected carriers, constitute incriminating evidence.

As no satisfactory treatment is known for contagious pleuro-pneumonia, and as apparently recovered animals carrying the virus are prone to suffer relapses, cattle shown, with a reasonable degree of certainty, to harbor the infection should be slaughtered. Definite history of a previous attack of the disease in a suspected carrier is ample evidence for its destruction.

3. The virus of equine influenza

Influenza, "pink eye" or "shipping fever," is a common and important disease of the equine species. It manifests itself as an acute, febrile contagion, characterized by a catarrhal inflammation of the mucous membranes, especially those of the head region. Further, inflammatory or edematous swellings in various parts of the subcutis and the tendons are common to the affection.

The etiology of the disease has been more or less obscure but in view of positive transmission experiments conducted by a number of investigators with filtered inoculums, it is generally accepted that the causative agent is a filterable virus.

Stallions which have recovered from the disease may harbor the virus in their bodies and infect healthy mares through coitus several months or even one or two years following recovery from the disease. Poels (48) was able to infect healthy horses through intravenous injections of filtered semen from a stallion which for a number of months had infected mares bred to it. Basset (49) demonstrated the blood of a horse which had recovered from an artificial inoculation, to be infectious for three and one-half months subsequently.

Habitat of the virus. Nothing is known regarding the habitat of the influenza virus in the body of carriers aside from the fact that, occasionally, it may be demonstrated in the blood and in stallions in the semen. Because of its presence in the blood it is undoubtedly eliminated periodically in the urine.

Detection and management. A stallion may readily be suspected of being a carrier of the influenza virus when there is frequent history of influenza in various mares which he serves. According to Hutyra and Marek (50) the disease invariably develops in from six to nine days where infection is brought about through coitus. The identification of a carrier of the influenza virus, however, is only established by the transmission of the disease to a normal animal through the inoculation of blood, semen, or other specimens from the suspected animal.

Animals known to harbor the influenza virus should not be permitted to come in contact with susceptible animals. Stallions shown to be carriers should not be permitted to serve mares.

Apparently no attention has been paid to the treatment of carriers, hence, there is no data available on the value of various drugs which might be employed with a view to eliminating the virus harbored by such animals. In Germany salvarsan and neosalvarsan have been extensively used in the treatment of equine influenza and its complications with apparently good results in a certain percentage of cases. In carriers of the influenza virus, especially valuable stallions, the use of salvarsan or other arsenical products may be of value in destroying the infection.

4. The virus of hog cholera

Occasional reference is made in the literature on hog cholera, to possible carriers of the filterable virus of the disease among apparently recovered hogs. Further, the so-called "runts" which have had a chronic type of the affection have often been considered carriers of the infection. There appears, however, to be no records of carrier investigations in hog cholera, definitely establishing the existence of true carriers of the virus.

Dorset (51) and his associates in experiments to determine whether or not several recovered hogs harbored the cholera virus, carried out exposure and inoculation tests with entirely negative results.

Hog cholera has undoubtedly been transmitted to healthy animals by "runts." From present information, however, it appears that when such animals are capable of disseminating the infection they are more likely to be actually suffering from the chronic form of the disease than harboring the virus as carriers.

While it is entirely possible that there are instances of real carriers of the hog cholera virus, at present we are without information on the subject.

CHAPTER XX

Conclusion

There exist among animals carriers of organisms of infectious diseases just as they are found among members of the human family. The problem in veterinary medicine, however, differs in many respects from that in human medicine.

As in the case of man, carriers among animals disseminate infection through their respiratory, intestinal and genito-urinary tracts, and indirectly through insects, but in addition we have milch animals harboring and eliminating organisms from their udders. Further, with food-producing animals the carrier problem does not always end with the death of the animal. Harbored organisms may be transmitted to man through meat or meat-food products.

Under natural conditions animals are obviously more intimately associated than human individuals, affording conditions under which the carrier functions most effectively. Then the scavenging propensities of various species promote the carrier problem. Hogs, various wild animals and buzzards, for example, are continually ingesting a vast variety of organisms, a number of which may persist in the intestinal tracts of such animals for variable periods of time, thus serving as a source of infection for susceptible species.

The large number of species of animals with marked variation in susceptibility to certain infectious diseases, often permits members of one species to serve as reservoirs of infection for animals of a more susceptible species. This is well illustrated in trypanosomiasis.

In carrier work in veterinary medicine an outstanding feature is the fact that serological tests can, in a number of instances, be employed to good advantage. While such tests may not differentiate the carrier from the case, and may miss some carriers, nevertheless in numerous cases these tests will narrow the problem

by identifying animals which are then, or have previously been, infected with a particular type of organism.

A notable feature of the carrier problem in veterinary medicine is the vast number of carriers in certain of the infectious diseases. In bovine piroplasmosis, for example, the great percentage of cattle in infected districts are, or have been, carriers.

In the control of carriers among veterinary subjects ability to slaughter animals harboring pathogenic organisms, where such procedure is feasible, is a distinct advantage. In addition, control is more perfect because the personal element is largely eliminated.

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